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Primary Pulmonary Tuberculosis in Adult.—A Sardinian, aged 31, living in Paris eight months, succumbed in less than fifteen days to an illness, the onset of which was sudden, and characterized by fever, pain in the side, cough and mucopurulent expectoration; and later the development of a meningeal syndrome and a terminal hemiplegia. At autopsy, generalized miliary tubercles were discovered in the lungs and viscera; besides, in the lower part of the right upper lobe of the lung, near the hilum, there was a small cavity of recent formation, about the size of a small nut, and in its immediate vicinity there was a large caseous tracheobronchial lymph node. There were no pleural adhesions or fibrous tubercles. It is believed that this is a case of primary-infection tuberculosis; this infection occurred after the patient's arrival in Paris, so that almost immediately after the formation of the chancre of inoculation, represented in this case by the cavity, a generalized tuberculosis is developed. —*Sur un cas de tuberculose pulmonaire de première infection chez l'adulte, A. Lemierre and E. Bernard, Meeting, Soc. Méd. d. Hôp. de Paris, November 21, 1924, reported in Presse Méd., November 26, 1924, no. 95, 941.*—(*B. T. McM.*)

Ghon's Primary Focus.—The primary foci of Ghon were found most often in the seventh or eighth right intercostal spaces, but also in other parts of the lung, and it is believed that they occur more frequently in adults and children than described. In the majority of cases there is a relation between the primary focus and the tributary lymph nodes. Since the primary focus can be the source of subsequent disease, an early recognition of the condition of the primary focus and its tributary nodes is of great significance for proper and early treatment.—*Der Primärkomplex, sein Nachweis und seine Bedeutung im Schwindsuchtsproblem, A. Spitz and W. Altschul, Beitr. z. Klin. d. Tuberk., 1923, lvii, 43.*—(*H. J. C.*)

Pathological Anatomy of Miliary Tuberculosis.—In order to study the relation of the exudative and productive processes in miliary tuberculosis of the lungs, the localization of tubercles in the lung, the type of older tuberculous lesions, the tissue reaction in miliary tuberculosis, and the clinical and anatomic pictures in 35 cases were carefully examined. The cases were divided according to anatomic findings into three groups, miliary tuberculosis (1) in the exudative stage, (2) in transition forms and (3) in the productive stage. It was found that exudative miliary tuberculosis is found in pure form only in acute, early cases, while typical epithelioid and giant-cell tubercles were found in the slow, protracted cases. The histological picture, as well as the location of the nodules and the tissue reaction, led to the conclusion that the granulation-tissue productive tubercles develop from the caseating, exudative, intraälveolar forms so that the sequence is exudation, caseation, productive reaction. In tuberculosis of the viscera the exudative stage remains in the background. The differentiation of older lesions is more definite with group 1 and becomes more difficult with groups 2 and 3. Resistance is greater in the second and third forms. Regarding the relation of the clinical picture to the anatomical findings it is believed that the so called "typhoid" forms are more of the exudative type. —*Beitrage zur pathologischen Anatomie der Miliartuberkulose, P. Huebschmann and A. Arnold, Virchow's Arch. f. path. Anat., 1924, ccxlix 165.*—(*H. J. C.*)

Pleural Annular Shadows.—That annular shadows appearing in the roentgeno-

grams of pulmonary tuberculosis may represent circumscribed pleuritic lesions is proved by the recent clinical and postmortem reports of Herbert, Rusk and Randolph, de Jong and Pestel, and Casellas; and these reports are reviewed. Casellas has also found such a lesion casting an annular shadow in a case of nontuberculous bronchopneumonia. Means of distinguishing pleural shadows from true cavity shadows are discussed. The tendency to call most doubtful annular shadows pleural is deprecated because under such indecisive circumstances the laws of chance favor cavitation. *Conclusions:* 1. Pleural annular shadows are realities which must be distinguished from intrapulmonary cavity shadows. 2. The lesion casting such shadows appears most often to be a subacute or chronic localized pleurisy which often undergoes rapid changes in size. This may be accompanied by a puckering, dimpling, or umbilication of the subjacent pulmonary tissue, and the resulting pleural interstice may contain a small amount of fluid. 3. In most instances pleural annular shadows can be identified by the methods of observation suggested.—*The Nature and Differentiation of Pleural Annular Shadows, J. B. Amberson, Jr., Am. J. Roentgenol. & Radium Therapy, November, 1924, xii, 438.*—(*B. T. McM.*)

Histopathology of Elastic Tissue of Cartilaginous Bronchi.—In the normal state the larger bronchi possess a triple protecting armature, an elastic, muscular and cartilaginous layer. The elastic layer is of greatest thickness in the intervals between the cartilaginous plates, and the general direction of the elastic fibres is longitudinal, while others are associated with the muscles of Reissessen in a direction perpendicular to the bronchial axis. The two principal longitudinal bundles are in the external and internal limiting membranes, with fibres ramifying among the blood vessels and bronchial lymph nodes. In fact, all the elastic fibres between these two limiting membranes form a perimuscular, periglandular, and pericartilaginous network, called the "intermediary network." Acute respiratory infections affect this elastic armature and may pave the way for later bronchiectatic changes. The two diseases which cause the greatest alteration, however, are tuberculosis and syphilis. The effects of chronic fibrocaseous tuberculosis are chiefly, at least in the beginning, localized. Syphilis, on the other hand, has a predilection for the bronchi, affecting profoundly their elastic tissue, and giving the picture of a bronchiectasis with irregular nodular dilatations. The bronchial lumen is enlarged, the walls invaded by sclerotic placques, and the structures are greatly distorted. The internal limiting membrane is most profoundly affected, the perichondrial network being most resistant. Elastic hyperplasias are less commonly seen in the course of pulmonary syphilis. *Conclusions:* Syphilis injures profoundly the cartilaginous bronchi, especially their elastic coat. A differential diagnosis from the lesions of tuberculosis is, in a general way, possible, although there is no certain pathognomonic distinction.—*L'armature élastique des bronches cartilagineuses a l'état normal et en histo-pathologie, M. Letulle, Presse Méd., August 30, 1924, no. 70, 713.*—(*A. P.*)

Calcification of Ribs in Relation to Pulmonary Tuberculosis.—The grade of calcification of the anterior ends of the ribs, the cartilaginous bony junctions and the rib cartilages was studied roentgenologically, and this was correlated with the pulmonary findings. The lime content varied within wide limits. There is a difference between the two sides of the thorax, as well as between the different ribs on the same side. The first-rib cartilage is most frequently calcified, and especially after the twentieth year. This leads to a loss of elasticity of the cartilage, and with this a lessened inflation of the apex. A coincident calcification of a number of ribs in early life is occasioned by the glands of internal secretion and the vegetative nervous system. In localized calcification or decalcification there exists a limited relation to the lungs in that over fresh tuberculous processes the lime content is diminished, while over healing processes it is increased. It is believed that this may be utilized as an additional aid for the determination of the activity of a tuberculous process.—*Der röntgenologische Kalkstatus des Brustkorbes im Zusammenhang mit tuberkulösen Erkrankungen der Lunge, K. Käding Beitr. z. Klin. d. Tuberk., 1924, lviii, 143.*—(*H. J. C.*)

Chronic Stasis in Lung and Collateral Blood Vessels.—In all chronic circulatory stasis in the lungs due to chronic (tuberculous) inflammations, there occurs the possibility of the formation of abnormal collateral vessels in the pleuritic adhesions between the pulmonary veins and the upper aperture (mammary) veins. Again, there can occur a dilatation of existing efferent vessels, especially the bronchial veins and their anastomoses with other veins (*pericardiacophrenica* and *V. oesophagea*). Experimentally the latter could be produced by partial occlusion of the pulmonary veins of one lung. Pertinent clinical observations were not made. Newly formed collaterals, especially

over the upper lobe as communications of pulmonary veins with branches of the internal mammaries, are of importance for the development of air emboli in the right heart. In all cases in which physical and roentgenological examinations of the thorax reveal stasis in a lung, there exists the possibility of abnormal collateral vessels. Special caution is then necessary in making diagnostic punctures or instituting therapeutic pneumothorax or pneumolysis. Horizontal posture of the patient with coincident bending down of the head is recommended. With the appearance of emboli, immediate discontinuance of the procedure at hand is advised. Wounds are then well tamponed. Low position of the head and cardiac stimulants aid in preventing evil consequences. Heart puncture and aspiration of the air from the right heart may be tried.—*Die Bedeutung chronischer Stauungszustände im Lungenkreislaufe für die Bildung abnormer Kollateralen in das Gebeit der oberen Hohlvene; zugleich ein Beitrag zur Frage der Luftembolie in den grossen Kreislauf und das rechte Herz, K. Schlaepfer, Beitr. z. Klin. d. Tuberk., 923, lvii, 98.*—(*H. J. C.*)

Resolution of Pulmonary Tuberculosis.—Three case histories, with reproductions of serial roentgenograms, are presented to correct opinion that one criterion of diagnosis of pulmonary tuberculosis is a certain fixity and persistence of shadow, and to bring out the fact that definite pulmonary tubercles may at times heal by resolution and disappear from the skiagram in a comparatively short time. Among other forms miliary tuberculosis of the lungs may heal in this way. In one of the cases reported artificial pneumothorax treatment was used; upon reëxpansion the lung was clear of disease except for a small scar at the site of a former cavity, healing having occurred chiefly by resolution. In such cases it is suggested that collapse of the lung brings about an overbalance of antibodies which prevents a further proliferative cellular reaction in the lungs but instead results in resolution. When pneumothorax is not used this overbalance may be produced by some other mechanism into which more than one factor enters. The impression is gained that resolution is more likely to occur in the exudative type of lesion. Possibly a residuum of increased lymphoid tissue may be left at the site of former tuberculous lesions. *Summary and conclusions:* 1. The pathological doctrine that healing of the lesions induced by the tubercle bacillus always signifies sclerosis or calcification ought to be revised somewhat; in a small number of such cases, at least, healing had been noticed to take place by resolution. 2. Cases of pulmonary tuberculosis are reported, and a number of their serial roentgenograms are presented to demonstrate the fact that definite tuberculous shadows may fade out gradually and disappear entirely from the X-ray plates. 3. The clearing and disappearance of tuberculous lesions may take place in miliary tuberculosis as well as in other types of pulmonary tuberculosis. Physical examination is of little value in detecting such changes; only by repeated roentgenographic observations can a correct prognosis be made. 4. These facts do not substantiate the opinion held by many roentgenologists that one criterion of diagnosis of tuberculosis is a certain fixity and persistence of shadow; it is the author's belief that a more systematic serial roentgenographic study of pulmonary tuberculosis would disclose a much larger percentage of instances of complete resolution, clearing and disappearance of tubercles.—*Resolution and Healing in Pulmonary Tuberculosis, R. A. Bendove, Med. J. & Rec., January 7, 1925, cxxi, 36.*—(*J. B. A.*)

Air Embolism in Pleural Puncture.—A case of lung abscess is reported, in which a rib resection was being performed and there resulted a short tonic convulsion, and the patient became pale and comatose, but slowly recovered. On the following day paresis of the right arm and leg developed, with patellar and ankle clonus, from which the patient recovered. It is concluded that the symptoms resulted from an air embolism, since an infectious embolus would have resulted in inflammatory changes of more permanent character in the brain.—*Luftembolie bei Pleurapunktion, P. Hornung, Beitr. z. Klin. d. Tuberk., 1923, lvii, 48.*—(*H. J. C.*)

Bronchiectasis in Pulmonary Tuberculosis.—A girl, aged 23, developed a subacute left pleuropulmonary tuberculosis: tubercle bacilli were present in the sputum. Pneumothorax could not be induced because of adhesions. Later, a bronchopulmonary sclerosis developed, with no cough or expectoration. Subsequently the sclerosis became more marked, the mediastinum was retracted, signs of cavity appeared, the sputum became profuse although negative for tubercle bacilli, and bronchial dilatations were demonstrated radiographically following the injection of lipoidol. Rist remarks that bronchiectasis is usually of bronchopneumonic or pneumonic origin, and only exceptionally of tuberculous origin.—*À propos d'un cas de dilatations bronchiques développées dans une sclérose pulmonaire avec symphyse pleurale consécutive à une pleuropneumonie tubercu-*

lose, E. Sergent, P. Pruvost and Cottenot, meeting, Soc. Méd. des Hôp de Paris, December 12, 1924, reported in Presse Méd., December 17, 1924, no. 101, 1009.—(J. B. A.)

Influence of Minimal Tuberculous Infection of Young Rabbits on Reinfection in Adult Life.—Fourteen rabbits, during infancy, were given small pulmonary tuberculous infections. Half of these, used as controls, showed no lesion due to the primary infection after they had reached the adult age. The other 7 were reinfected with minimal doses of bacilli by the same route when they had attained adult life; all these presented lesions, in some cases discrete, in others marked, although in 4 cases the total dose of bacilli employed for the two injections was ten times weaker than the primary infection of the control rabbit. It is concluded that in the rabbit slight infection of infancy, which is capable of healing, does not render the lung allergic. Instead of acting as a vaccination, it predisposes, on the contrary, to reinfection which evolves like the clinical type of caseous tuberculosis of first infection.—*Action de l'infection pulmonaire tuberculeuse minime du lapin jeune sur la réinfection à l'âge adulte, A. Philibert and F. Cordet, meeting, Soc. de Biologie, December 13, 1924, reported in Presse Méd., December 17, 1924, no. 101, 1009.—(J. B. A.)*

Physiology of Bilateral Pneumothorax.—Experiments on dogs, cats and rabbits are reported after a careful review of the literature. Open bilateral pneumothorax is tolerated by dogs, provided the diameter of the pneumothorax openings are smaller than one-half the diameter of the main bronchus. In all cases after changing a narrow open pneumothorax into a closed pneumothorax there resulted an immediate improvement in the condition of the animals. The severe asphyxia resulting in a bilateral, wide open pneumothorax immediately disappeared if both openings in the thorax were closed at the height of inspiration. Bilateral narrow open pneumothorax had the same course, regardless of whether this form occurred in a previously uninjured thorax or followed a wide opening in the thorax. Bilateral closed pneumothorax has a milder course than a bilateral narrow open pneumothorax, regardless of whether the closed pneumothorax follows a shorter or longer period of existence of a narrow open pneumothorax, or a wide open pneumothorax. Respiratory excursions of the thorax in dogs are more vigorous than normal in closed or narrow open pneumothorax. The respirations are of greater depth and are increased in frequency. They are more marked in narrow open and less so in closed bilateral pneumothorax. In wide open pneumothorax the respirations rapidly take on an asphyxial character. In the early periods they differ mainly from the normal by their marked increase in depth. In closed and narrow open pneumothorax, in spite of increased intrapleural pressure, there are still at times satisfactory hypercompensatory changes. With absorption of the pleural air normal intrapleural pressures develop in the parts free from adhesions. The total respiratory exchange in bilateral pneumothorax in dogs is sometimes less than normal, at times, however, exceeding the normal. The percentage of exhaled CO_2 and inhaled O in bilateral pneumothorax is usually less, but since respiration is more frequent the total exchange per hour not only attains normal but may exceed it. In certain cases bilateral pneumothorax is more comfortable than monolateral. Many of the uncomfortable features of monolateral pneumothorax are explained on the basis of a displacement and paradoxical movement of the mediastinum. The blood pressure increases somewhat during the time of pneumothorax formation and it may remain high or drop to normal. The author hopes that his observations will encourage attempts to operate on bilateral pleural and pulmonary conditions.—*Pathologische Physiologie des doppelseitigen Pneumothorax, M. Friedland, Beitr. z. Klin. d. Tuberk., 1924, lviii, 1.—(H. J. C.)*

Influence of Nonspecific Proteins on Leucocytes in Tuberculosis.—The influence of nonspecific proteins (*Yatren, Casein*) on the blood picture of tuberculosis was studied with the following results: In inactive tuberculosis the leucocytes and eosinophiles slightly increased, while in progressive cases the leucocytes only slightly increased and the eosinophiles may even decrease. It is concluded that these observations only give information on the reaction powers (probably of the bone-marrow) to specific irritants on the day of the examination. Repeated examinations correlated with the clinical picture, give valuable prognostic information.—*Über die Beeinflussung des Blutbildes durch unspezifische Reize bei den verschiedenen Formen der Lungentuberkulose und ihre Bedeutung für die Prognose, O. Seitler, Beitr. z. Klin. d. Tuberk., 1924, lvii, 480.—(H. J. C.)*

Relation of Endocrine Glands to Natural Immunity.—The natural immunity of various animal species to disease has not been clarified by experimental

investigation. The difference between the behavior of the rabbit and the guinea pig to different types of tubercle bacilli is well known. Toward typhus the guinea pig is very susceptible, while the rabbit is relatively resistant. The rabbit is susceptible to syphilis, and the guinea pig is immune. An attempt was made to work out a scheme of the organs of internal secretion for the animal species, or an "endocrine formula." Guinea pigs, rabbits and gray rats were studied by the method of Beneke, based on the weight and size of the organs. According to this, the function of the normal organ increases with its weight increase, and decreases with a lessened weight. In rabbits the weight of the thymus is greatest, being 8 times that of the thyroid, and 3 times that of the adrenal; the adrenal, next in size, is 3 times larger than the thyroid; and last comes the hypophysis. In the guinea pig the thymus is one and a half times smaller than the thyroid, and sixteen times smaller than the adrenal, the adrenal being largest, and the hypophysis smallest. In the human being the average weight of the organs varies as follows: up to the sixth or seventh year the thymus is largest, the adrenal next, the thyroid next and the hypophysis smallest; up to fifteen to sixteen years the thymus is largest and following in order are the thyroid, adrenal and hypophysis; with the involution of the hypophysis the thyroid takes first place and the thymus the last. The rabbit agrees most nearly with the child up to the sixth year of age. The formula of the adult agrees best with that of the guinea pig. It is assumed that the biological individuality of the rabbit, in comparison with the guinea pig, is essentially related to the marked preponderance of the thymus in the rabbit's endocrine formula. The question is raised of whether the characteristics of the natural immunity of these animals cannot be a part of the constitutional make-up, and especially the endocrine formula. The behavior of man, rabbit and guinea pig toward the various types of tubercle bacilli is here considered. In adult man the bovine type is rarely found, while in children it is relatively frequent; the rabbit is especially susceptible to the bovine and little susceptible to the human type; while the guinea pig is equally susceptible to both. Transmutation of one type into the other is possible. This is of special significance when we view the fact that the rabbit and the child are constitutionally closely related, while the guinea pig more nearly approaches the adult, but at the same time resembles a child in the relation of adrenal, thyroid and hypophysis to each other. A similar relation exists toward typhus: for the adult high mortality, for children slight mortality. The guinea pig behaves toward typhus like the adult, and the rabbit like the child. These relationships make it seem possible that the different behavior toward tuberculosis and typhus, of the rabbit and child on the one hand and the guinea pig and adult on the other, is constitutionally occasioned by the thymus gland.—*Zur vergleichenden Erforschung der Formeln für die endokrinen Drüsen des Meerschweinchens und Kaninchens im Zusammenhang mit ihren biologischen Eigenschaften, A. Sternberg and S. Pojorowsky, Beitr. z. klin. d. Tuberk., 1924, lvii, 402.*—(*H. J. C.*)

Influence of Tuberculin on Secretion of Adrenalin.—The blood plasma of cases of pulmonary tuberculosis contains a vasoconstrictor substance identified with adrenalin. How does this pathological hyperadrenalinemia occur in pulmonary tuberculosis. Tuberculin calls forth an increased secretion by the adrenals in rabbits. The tuberculin acts peripherally, since, after exclusion of the preganglionic nerve fibres by means of nicotine, a hypersecretion can still occur. The blood for examination was obtained from male or nonpregnant female rabbits, according to the method of Stewart and Rogoff, from the suprarenal vein, and its vascular action as oxalate plasma tested on a Läwen-Trendelenburg frog. The operation itself does not influence the secretion of the adrenals nor does the injection of protein-containing thymus extract do so. After tuberculin injection there is an outspoken increase in vasoconstrictor substances in the rabbit's blood.—*Über den Einfluss Tuberkulins auf die Adrenalinsekretion der Nebennieren, M. Osawa, Archiv. f. exp. Path. u. Pharmakol., 1924, ci, 249.*—(*H. J. C.*)

Blood Calcium in Tuberculosis.—The free calcium content of the blood serum of 30 tuberculous patients was studied. The oxalate method was used. This method, in normal subjects, gave values between 110 and 115 mgm. per litre. All the patients also gave values of over 100; but, while in the severe cases they were always between 100 and 110, in those in good general condition they were found to be between 120 and 130 mgm. per litre.—*Recherches sur la calcémike des tuberculeux, E. Sergent, L. Binet, and M. Bagliano, Section d'étude, scientifiques d. l'Oeuvre d. l. Tuberculose, June 14, 1924, reported in Rev. d. l. Tuberc., August, 1924, v, 547.*—(*A. P.*)

Calcium Exchange in Tuberculosis.—A number of observed facts have served to

show that lime impoverishment of the body favors its tuberculization, and Teissier, in 1876, called attention to what he regarded as defective mineral exchanges in the tuberculous. The majority of French writers believe that there is a decalcification at the beginning of the disease, which later ceases. Most of the German writers, excepting Ott, believe that decalcification is exceptional, and, when it occurs, usually terminal. Steinitz and Weigert, Schetelig and A. Meyer see no evidence of any decalcification. Studies based entirely on urinary calcium should be rejected as misleading. Ott's studies are also unsatisfactory, in that he has not compared phthisical with healthy individuals under the same conditions. His results, however, appear to show the inability of the tuberculous properly to balance his exchange with the normal calcium ration and inability to store lime with a diet rich in calcium. Sergent has proposed adrenalin-calcium medication: although the urinary calcium output diminishes under it, the intestinal output increases. The following conclusions are reached concerning various remedies employed: 1. Calcium chloride and lactate not only lead to no gain in body calcium, but even a loss, while the carbonate and glycerophosphate, as well as the triple phosphate, are unassimilable. 2. Thymic extract, reputed to aid in calcium fixation, gives negative results. 3. A diet rich in milk, which contains 3 gm. calcium per litre is recommended. 4. The addition of parathyroid extract in doses of 0.02 gm. per day appears to prevent decalcification and assist in calcium deposition. *Elimination of calcium:* An acid-forming diet, such as one rich in meat, will increase the urinary calcium output at the expense of the fecal. Addition of sodium chloride has a similar effect. On the other hand, an alkaline or vegetarian diet reduces the urinary output of calcium but increases the fecal. Most of the calcium output is in the form of phosphates. The blood calcium is maintained fairly constantly at 100 to 120 mgm. per litre. *Calcium metabolism:* If the diet is deficient in calcium, as was the case in Austria during the war, one sees osteoporoses, or "famine osteopathies" which are cured by adding sufficient calcium to the diet. In the tuberculous, as in the rachitic and those suffering from tetany, the trouble is not so much calcium deficiency as impairment of the power of fixation. The importance of the parathyroids in calcium metabolism is well known, and MacCallum has applied the term "calcic diabetes" to the condition which follows their removal. Besides glandular secretions, vitamines, cod-liver oil, and light, solar or ultraviolet, affect this fixation. Sherman, in the United States, has found many of the ordinary dietaries deficient in calcium and has advised, where sufficient milk cannot be had, the addition to the table salt of calcium carbonate or phosphate.—*Étude expérimentale des échanges calciques chez les tuberculeux, Critique expérimentale des procédés de recalcification, E. Manoussakis, with discussione by M. P. Weill, Section d'études scientifiques d. l'Oeuvre d. l. Tuberc., June 14, 1924, reported in Rev. d. l. Tuberc., August, 1924, v, 541.*—*(A. P.)*

Blood-Serum Calcium in Tuberculosis.—The irritability of the vegetative nervous system in tuberculosis results in disturbances of the calcium content of the tissues and blood. The amount of free calcium ions cannot be determined accurately in the blood. In order to study the relationship between calcium metabolism and the various forms of tuberculosis, the total calcium content of the blood, according to the method of DeWaard, was determined on 45 tuberculous patients. Twenty of these cases, including the various forms except the exudative, had a normal serum calcium content (10.5 to 11.5 mgm. per cent), and there were no marked disturbances of the vegetative nervous system. In 8 of the cases there were high values (11.5 to 12 mgm. per cent). These values were found mostly in productive tuberculosis of wide extent, while normal values were exceeded in favorable or fibroid cases. Among the 8 cases with hypercalcemia there was one patient with an active acinous-nodose process and increased irritability (especially vasomotor lability). Aside from this there were 3 cases with hyperirritability. Hypocalcemia was found in 9 patients, one of an asthenic type with inactive fibrotic tuberculosis. Six in this group had hyperirritability, with prominent vagotonic symptoms, and 4 of them an exudative tuberculosis of severely destructive type. One of the cases with low blood calcium was an old inactive indurative case with calcified upper-lobe tuberculosis. Besides the serum calcium determinations, the globulin precipitation reaction of the serum, according to Matefy, was performed, and marked globulin increases were found in the exudative tuberculosis cases. There was no direct relationship between the relative globulin increase and the calcium, and none between these and the degree of allergy to tuberculosis.—*Tuberkulose und Serumkalkspiegel, F. Krömeke, Beitr. z. Klin. d. Tuberk., 1924, lvii, 467.*—*(H. J. C.)*

Immunobiology of Tuberculosis.—The Besredka antigen is a very valuable aid in

the clinical diagnosis of tuberculosis. A useful preparation may be obtained from solid media. In 500 sera examined, in cases in which tuberculosis was present in the viscera, 94.7 per cent of positive reactions were obtained. A negative Besredka reaction may occur in incipient tuberculosis, after cure, and in the moribund state. In bone tuberculosis the reaction is frequently negative (60 per cent of the cases examined in this investigation). In cases in which tuberculosis is not clinically demonstrable, in the absence of syphilis, positive reactions are rare (2.5 per cent). In syphilis, with Wassermann reaction positive, in the absence as well as presence of tuberculosis, 90 per cent positive reactions occur. The reaction therefore has no value as a means of diagnosing tuberculosis in the presence of syphilis. In tuberculosis, in the absence of syphilis, the Wassermann reaction is usually negative. The antibodies concerned in the Besredka reaction can be demonstrated in the pleural fluid in tuberculous pleuritis and in the spinal fluid in tuberculous meningitis. Malaria has no influence on the Besredka reaction. Old tuberculin is a far less effective antigen than the Besredka antigen in the complement-fixation reaction of tuberculosis, even in cases in which tuberculin has been used in treatment. There is no relation between the Wassermann reaction and positive complement fixation with old tuberculin as antigen. In experimental tuberculosis antibodies can be demonstrated in the blood by means of the Besredka antigen as early as 7 to 9 days after the infection, but the titre never reaches a great height, and rapidly decreases with the waning of the active tuberculous process. Antibodies can rarely be recognized by the use of O. T. as antigen. Immunization of healthy guinea pigs with O. T. leads to the production of no antibodies which can be recognized by complement fixation with either the O. T. or Besredka antigen. On immunization of both healthy and tuberculous guinea pigs with the Besredka antigen a rapid production of antibodies occurs. The amboceptor titre in the serum of tuberculous patients is not high. With the usual serum dose of 0.2 cc. many reactions are negative in cases in which a positive reaction occurs with the use of 0.4 cc. The Besredka antigen, being a homogeneous bacterial emulsion, is suitable as an antigen for the demonstration of agglutinins. Agglutinins are produced in the serum in tuberculosis only in very small amount. No relation is apparent in the amount of amboceptor and agglutinin. Usually agglutinin reaction may be positive in a serum dilution of 1:10, rarely in one of 1:100. A positive agglutination reaction with 1:10 serum dilution has clinical value for diagnosis, but a negative reaction does not exclude tuberculosis. The Matefy flocculation reaction in tuberculosis, although not specific for tuberculosis, has diagnostic and prognostic value. It bears the same relation to the Besredka complement-fixation reaction that the flocculation reactions in syphilis do to the Wassermann reaction. In 260 Besredka-positive sera examined the Matefy reaction was positive in 76 per cent. The addition of glycerol as a preservative does not render serum unsuitable for the Besredka test. Experimental infection of guinea pigs with very small doses of living tubercle bacilli protects them against later lethal doses. Following such infections the Besredka reaction is positive for a period during which the disease is active, and then becomes negative. It remains negative after reinfection. Immunization of guinea pigs with large amounts of O. T. confers no protection against infection with living tubercle bacilli. Immunization with the Besredka antigen, which calls forth intense antibody production, appears to confer some protection against infection. Treatment of tuberculous guinea pigs with the Besredka antigen seems to prolong life, treated animals living about a month longer than nontreated controls. In guinea pigs immunized with the Besredka antigen massive infection may lead to marked anaphylactic symptoms and sudden death, whereas similar infection of normal animals leads to no immediate reaction. The author concludes that the Besredka antigen should be studied for its protective and curative value in human tuberculosis.—*Experimentelle Beiträge zur Frage der Immunobiologie der Tuberkulose, L. Horowitz-Wlassowa, Ztschr. f. Immunitätsforsch. u. exper. Therap., Jan. 2, 1925, xlii, 1.*—(*E. R. L.*)

Allergic Irritability.—In a previous paper, "allergic irritability" was defined as a "general characteristic of the animal on the basis of which it reacts to stimuli of the antigenic class, whether they be helpful, injurious, or indifferent to bodily health." It has also been shown by Wright and Lewis that variations in the natural immunity or resistance to tuberculosis in guinea pigs are partially determined by inheritance. The observation is now reported that these animals vary by families in their anaphylactic reactions. Four inbred lines of guinea pigs cited by number in order of decreasing resistance to tuberculosis as follows, 35, 2, 13 and 39, were used in the investigation. Previously untreated animals were sensitized with washed red blood corpuscles of the sheep and later given a second injection or shock dose. Family 35 showed fewest

anaphylactic reactions (9 animals giving two slight reactions), whereas 2 and 13 showed progressively more, and in family 13, out of 8 animals tested, there were deaths within two hours. The titre of the antisheep amboceptor in the different groups was found to parallel the severity of the anaphylaxis. The following determinations were noted: Family 35, 1/374; family 2, 1/455+; family 32, 1/600; and family 13 1/693. Similar results with regard to anaphylaxis were obtained with horse serum, family 35 giving the least number of reactions and family 13 the most. Family 35 appears to be definitely more resistant to this general form of intoxication. In the horse-serum experiment, family 35 manifested the same reaction as the usual crossbred stock of guinea pig. In an experiment, devised to determine the rate at which families become sensitive, the same relationship was observed with regard to families 35 and 13, the latter showing a much earlier sensitization than the former. An evaluation of the observed parallelism between the resistance to horse-serum anaphylaxis and that to tuberculosis must be reserved. It may be recalled, however, that the tuberculin reaction, which seems to be so very important as a feature of infection with the tubercle bacillus, is a reaction of hypersensitiveness, and it is not difficult to imagine that further work may justify placing more emphasis on the relationship here developed. *Conclusions:* Inbred lines of guinea pigs which have previously been observed to differ in their susceptibility to tuberculosis differ in their anaphylactic responses as well. The families that are relatively resistant to tuberculosis appear also to be somewhat more resistant to some one or more of the phases of the anaphylactic reaction-complex.—*Allergic Irritability. II. Anaphylaxis in the Guinea Pigs as Affected by the Inheritance, P. A. Lewis and D. Loomis, J. Exper. M., March 1925, xli, 327.*—(*J. S. W.*)

Pulmonary Changes of Allergy—Tuberculous reinfection in the lungs has been studied by a number of authors. Bezançon and de Serbonnes, in 1914, reinfected guinea pigs intratracheally, and in two instances observed extensive cavity formation, although the more usual lesions are those of chronic alveolitis and interstitial pneumonia, and Philibert and Cordey found the lesions usually proportional to the sum of the doses, often ending in the production of massive caseation and great cavities. When rabbits are first inoculated subcutaneously, the lesions of subsequent intratracheal infection are extensive, generalized, and tend to caseation. The experiments reported here were performed on guinea pigs, the injection being made directly into the exposed trachea. Homogeneous liquid cultures of human bacilli were employed, heated to different temperatures, and also cultures on potato medium killed at 110°. Reinoculation was done after three or four weeks with 0.01 gm. of virulent bacilli in normal serum. The chief disturbing factor was the occasional ejection of the injected liquid by coughing. Some animals died two months after reinfection; those which survived were killed at the fifth month. The later the animals died, the less severe the lesions found. Those dying early constantly showed very intense lesions, such as massive caseation, often progressing to cavitation. The reinfected animals reacted in a special way, namely, with a tendency toward the production of massive caseation and cavitation of all degrees.—*Sur le phénomène de Koch pulmonaire. Infection et réinfection tuberculeuse intrachéales chez le cobaye F. Arloing and A. Dufourt, Section d'études scientifiques d. l'Oeuvre d. l. Tuberculose, March 1, 1924, reported in Rev. d. l. Tuberc., June, 1924, v, 399.*—(*A. P.*)

Hepatic Anergy in Tuberculosis.—Fiessinger and Brodin in 1922, in an article abstracted at that time, advanced the claim that a chronic nontuberculous affection of the liver may suddenly aggravate a walled-off tuberculosis and favor a miliary spread of the disease through a weakening of the body's defensive mechanism. They also stated that a negative cutireaction to tuberculin is usually brought about in cases of liver insufficiency, and proposed the use of the term *hepatic anergy.* In March, 1924, *Daniello,* took exception to many of the ideas of Fiessinger and Brodin who now in their second paper advance new clinical observations to support their original contentions.—*À propos de l'anergie hépatique dans la tuberculose, N. Fiessinger and P. Brodin, Ann. de. Méd., July, 1924, xvi, 46.*—(*W. B. S.*)

Nature of Bacterial Allergies.—Two distinct types of hypersensitiveness may result from the contact of bacterial materials with the animal body. One of these, true protein anaphylaxis, in all likelihood plays a relatively slight rôle in the phenomena of bacterial invasion and resistance. The other, hypersensitiveness of the tuberculin type which appears early in the course of infection, has gained fundamental significance in view of the accumulating evidence which points to a definite relationship of this type of "allergy" with immunity and resistance to superinfection. The basis of the

tuberculin reaction cannot be explained as an antigen-antibody phenomenon, for the inciting substance (tuberculin) is not an ordinary coagulable protein and is not altered by heat or by repeated alcohol precipitation. Anaphylaxis to tuberculoprotein may be induced in guinea pigs by repeated injections of tubercle-bacillus extracts, but these animals rarely become tuberculin-sensitive, except possibly those treated with the nucleoprotein fraction. Conversely, infected guinea pigs are tuberculin-sensitve two weeks after infection without showing any evidence of being anaphylactic. Typical tuberculin-sensitiveness is apparently dependent on actual infection with bacilli, and not upon the successive injection of dissolved bacillary extracts. Attempts were made to produce the tuberculin reaction (skin test) passively. Guinea pigs inoculated with serum from rabbits intensively treated with autoclaved alcohol-ether treated human tubercle bacilli, failed to react to intracutaneous injections of O. T. 1/10. Yet this rabbit serum possessed a relatively potent precipitating titre for tuberculin. But when rabbits were treated in addition with live tubercle bacilli, or received these alone, with their sera it was found possible to transfer this form of allergy. Guinea pigs receiving such sera usually showed a definite reaction within five days, provided multiple, well developed, and not too advanced lesions were present in the rabbits. Similar reactions were obtained from injections of sterile filtrates of crushed tuberculous tissues (subcutaneous lesions) from rabbits, furnishing the serum. A few experiments were also successfully performed with crushed tissues from tuberculous guinea pigs. In addition to this direct investigation experiments upon passive sensitization with pneumococcus antiserum were done on guinea pigs using pneumococcus bacterial "residue" as the testing agent. The "residue" is the biologically active substance remaining after removal of nucleoprotein and coagulable protein. It is capable of being powerfully precipitated in vitro by the antipneumococcus serum. In the large majority of the animals no indications of delayed skin reactions of the characteristic tuberculin type were obtained. The above experiments would indicate that allergy, such as the tuberculin phenomenon, is not due to a reaction within the animal body between the antibody in the serum and the nonprotein residue material, with which they cause precipitation in the test-tube. Such results naturally encourage a resumption of chemical studies of the antigen, inasmuch as they again suggested the possibility of there being two separate materials in crude tuberculin, one concerned with the precipitin reaction, the other particularly important in regard to specific tuberculin hypersusceptibility or allergy. An attempt was made to separate these fractions by more complete precipitation of protein. It was thus possible to obtain two fractions, one of which, the residue, contains the materials precipitated by antiserum and almost free from allergy-inducing substances; the other, the so called nucleoprotein fraction, containing very little material precipititable by the immune sera, but representing the bulk of the allergy-inducing substance. The tuberculin reaction thus depends on something associated with the inflammatory reactions taking place about the lodgment of living or dead tubercle bacilli. Two possible mechanisms may be considered to explain this. On the one hand we can assume that a definite tissue reaction is necessary to liberate from the bacteria the materials which then are absorbed for general active sensitization of the body as a whole. On the other hand, it may be possible that the reacting antisubstance is produced locally in the course of the tissue reactions and passes out from this, passively sensitizing the rest of the body. That this latter process is probably an important part of the phenomenon is indicated by the facts that tissue extracts of the lesions, as well as an occasional serum, will transmit hypersensitiveness. It is evident that there is a fundamental difference between the results of immunization with coagulable proteins like horse serum, egg albumin, etc., and those observed with bacteria. The tuberculin reaction in all probability represents a principle widely applicable to all bacterial infections, for it shows a close analogy with the mallein, typhoidin, and abortin reactions. For the development of such allergies, however, it is not sufficient that dissolved or soluble bacterial materials be administered, but there seems to be required an actual tissue reaction in contact with the invading microörganisms. The mechanism by which such a reaction leads to the development of allergy is as yet obscure, but it is certainly not the ordinary antibody-antigen reaction. If we believe that the allergic state and increased resistance are parallel and perhaps causally related phenomena, the obvious inference arises that these substances upon which allergy depends may possess protective functions different from and based on a different mechanism from those possessed by antibodies.—*On the Nature of Bacterial Allergies, H. Zinsser and J. H. Mueller, J. Exper. M., January 1, 1925, xli, 159.*—*(J. S. W.)*

Characteristics of Tubercle Bacilli.—As there seems to be only one serological type of tubercle bacillus, immunity developed in response to the inoculation of one strain should protect against all strains. It is very necessary, in considering the results of immunity experiments, to guard against the assumption that immunological reactions, which can be demonstrated in the test-tube, constitute a useful index (or indeed any index) of true immunity to infection. Such results cannot be accepted without overwhelming evidence obtained by other means of inquiry. In any laboratory study of disease of bacterial origin the following points are of prime importance: (1) the mechanism of invasion that determines infection, and (2) the mechanism of disease production, and the mechanism of death resulting therefrom. A number of experiments are described, designed to elaborate methods whereby the disease produced in guinea pigs by inoculation with virulent cultures should be rendered sufficiently chronic to allow of therapeutic experiments being carried out, and to test the prophylactic and therapeutic value of antigens prepared by a variety of methods. The following experiments are first described: (1) An attempt was made to immunize guinea pigs with partially defatted tubercle bacilli such as were used in the preparation of the previously described agglutinating serum. In no stage of their preparation had these bacilli been exposed to a temperature higher than 30°C. Animals inoculated with multiple, increasing doses of these ether-acetone extracted tubercle bacilli were later infected with living human bacilli. Some of these animals were given a later further course of immunization. Compared with the controls, the treated animals showed no appreciable degree of immunity, and yet much smaller doses of the same partially defatted antigen calls forth an *agglutination response in rabbits*. (2) Tuberculous tissue, extracted by alternating freezing and thawing, both readily infected guinea pigs, and in no way influenced the course of the disease when used for treating guinea pigs already infected with tuberculosis. (3) The virulence of tubercle bacilli, exposed to sodium oleate, was found to be only slightly lower than that of untreated bacilli and the results reported by Noguchi could not be confirmed. The main difficulties in investigating infection centre around the question of dosage and virulence: (a) if too large a dose of an infecting germ is given, no prophylactic or therapeutic measure will save the animal; (b) if a dose sufficiently small or a larger dose of a bacillus of sufficiently low virulence is given, a certain number of control animals survive so long as to interfere with the final interpretation of the results obtained; (c) the infective capacity of a given strain varies from culture to culture; and (d) occasionally a large percentage of the material inoculated may consist only of dead bacilli. The last difficulty can be overcome to a large extent by using only rapidly growing cultures not more than three weeks old. The third difficulty, the variation in virulence, cannot be overcome entirely, but its influence may be partially eliminated by using strains not more than a year old, and by introducing a sufficient number of control animals into all experiments. Although they grow readily and are easy to handle, strains of low virulence should not be employed in experimental work. They are but poor representatives of the tubercle bacillus. The difficulty arising in the administration of small doses of the bacillus is largely that of mensuration, for cultures cannot be readily homogenized, so that dilution is liable to result in a very unequal distribution of the bacilli in the menstruum in which they are suspended. To partly overcome this difficulty, experiments were done in which a large dose of bacilli was administered so that absorption took place slowly. The object was to obtain a "depot action" from the inoculum, instead of the "pole-axe" effect that results from the inoculation of saline suspension of the bacillus. Virulent bacilli were ground up in olive oil and in 20 per cent tetraline in olive oil. Such material, in three parts, which received twenty-four, forty-eight and ninety-six hours incubation, respectively, was inoculated into a small group of guinea pigs with suitable controls. The animals infected with the ninety-six hour incubated material failed to develop tuberculosis. In the other two series, the test animals far outlived the controls, and those receiving bacilli treated with olive oil plus tetraline lived the longest of all. All showed tuberculosis except one of the latter. In this experiment the "depot action" sought was not obtained, but it is believed that such a procedure presents a simplified technique for carrying out Webb and Williams's experiment (prophylactic vaccination with carefully graduated doses of living virulent bacilli). This method also places in our hands a means of producing chronic tuberculosis in the guinea pig by inoculation of virulent cultures. It was noted that fairly extensive tuberculosis can occur in the guinea pig without much more loss of weight, and, therefore, those experiments which claim that a normal increase in weight is indicative of cure, must be accepted with great reserve. The nature of the disease seems to depend very greatly

on the dose of the infecting bacillus; the smaller the dose the greater being the tendency to chronicity. The mechanism of the action of the olive oil is probably dependent on both physical and chemical influences. Finally, a variety of substances were tested out on tuberculous guinea pigs in an attempt to demonstrate therapeutic activity. Guinea pigs which had received a heavy infecting dose (2 mgm.) of human bacilli were treated with the following substances: olive oil, olive oil plus 20 per cent tetraline, crude Wassermann antigen, Dreyer's (diaplyte) vaccine, and refined Wassermann antigen. The result of the experiments showed that in all these series the animals treated by the crude Wassermann antigen outlived those treated by the other methods, but the length of time which these survived is insufficient to allow of any conclusion being drawn. Crude Wassermann antigen consists of tubercle bacilli treated with tetraline until microscopic examination shows that the bacilli are no longer acid-fast. This material was diluted in olive oil for inoculation. Although the dosage of the therapeutic substances employed may have been unsuitable, being simply chosen at random, it was felt that in each instance it was sufficiently large. *Conclusions:* 1. Methods are described for the isolation of tubercle bacilli directly from sputum and morbid exudates (part I). 2. A serological survey of tubercle bacilli isolated from human sources shows that these all conform to one serological type (part II). 3. Average weekly weighing does not give one a true index of whether an animal is or is not suffering from tuberculosis. 4. Chronic tuberculosis can be produced in guinea pigs with virulent tubercle bacilli provided the dose is sufficiently small. 5. The weight charts alone cannot be regarded as of much value as an index in therapeutics. 6. There is no evidence that any of the antigens employed exhibited therapeutic qualities. 7. Methods are described whereby it may be possible to repeat the experiments of Webb and Williams with a simple technique.—*The Bacteriological Characteristics of One Hundred Strains of Tubercle Bacilli Isolated from Sputum (Section III), W. J. Tulloch, W. T. Munro, G. R. Rose and W. M. Cumming, Tubercle, December, 1924, vi, 105.*—*(J. S. W.)*

Metabolism of Tubercle Bacillus.—The metabolism of the tubercle bacillus has been studied, particularly in two of its phases. One has to do with its synthetic activity, in which the simple food elements of the culture medium are modified for structural purposes, and the other includes the catabolic processes by which the complex substance of the bacillus is broken down and excreted into the medium. The wax of the tubercle bacillus is an important product of its synthetic activities. The most conspicuous nutritional requirement of the bacillus is that for glycerol, growth rarely taking place without the presence of this substance. The synthesis of the wax is probably intimately bound up with the "glycerophilism" of the bacillus, for avirulent relatives of the tubercle bacillus similar in staining properties, which grow well in the absence of glycerol, also develop far less wax. Conversely, it has been found that a list of bacilli of the acid-fast group arranged in the order of their waxy content is also approximately arranged in the order of their apparent need for glycerol. Certain sugars can replace glycerol, although growth is much lessened and the lipin content reduced. The chemistry of the synthesis of complex wax from simple glycerol is unknown. It is well known that the wax present in the tubercle bacillus is concerned in acid-fastness, the wax itself being acid-fast; yet this peculiarity of the wax cannot be the direct cause of the acid-fastness of the bacillus, for the bulk of the wax can be readily removed without the staining property being affected. Furthermore, grinding the bacilli to a fine powder, a process in which none of the wax is removed, destroys acid-fastness completely. It would seem that acid-fastness depends on a relative impermeability of the bacillary protoplasm to the substances used in destaining. This impermeability is probably due to a peculiar physical or chemical combination of the lipin with the protein of the bacillus. With regard to the digestion of the bacillus, the separation of this lipin from its protein combination is a result much more easily achieved than the digestion of the wax alone under any conditions; and it is undoubtedly fully as effective in modifying the permeability of the bacterial body. A recent study on the chemistry of the tubercle bacillus has resulted in settling definitely the type of nucleic acid present. Johnson and Brown find that tubercle-bacillus nucleic acid is of the animal type and not of the plant type. Like other bacteria, the tubercle bacillus is able to thrive on nitrogen supplied in the simplest form. Ammonia, amino acids and acid amides are all suitable as sole sources of nitrogen for its growth. The bacillus possesses both the capacity for de-aminizing amino acids, and also of utilizing the ammonia thus formed for structural purposes. The presence of both citrate and iron is useful for promoting the growth of tubercle bacilli, and other polybasic acids seem likewise to have a favorable

action. The formula of medium on which bacilli have been found to grow luxuriantly is given. In the course of growth of the tubercle bacillus in laboratory culture media, changes in reaction take place. While both strains lead to an initial alkalinity in glycerol broth, the bovine-type culture remains alkaline, or perhaps returns to the original reaction, while the human-type culture after some weeks becomes progressively acid. These changes have been utilized as a means of distinguishing types of bacilli, but, as many exceptions are known to occur, rabbit inoculation remains the surest means of making this distinction. The change in the reaction of the media may be easily recognized and measured by adding a suitable indicator for color comparison. A brief résumé is given of the theories as to the nature of the tuberculin reactions. The majority of observers distinguish the type of allergy concerned in the reaction from true anaphylaxis, and refer to it as the "hypersensitiveness of infection." It would seem that this peculiar sensitiveness to tuberculin is conferred only by infection with the living microörganism concerned, although a more or less transient hypersensitiveness occurs following the injection of dead bacilli or their bacterial proteins. The active principle of tuberculin is nonantigenic in normal animals, although tuberculoprotein, like any other complete protein, will sensitize an animal so that anaphylactic shock may be observed. Tuberculin, according to Selter, acts in the unchanged condition and only as a specific irritating substance affecting sensitized tissues, and produces inflammation in them without itself being changed or bound to the tissues. Krause points out that the constitutional symptoms of the tuberculin reaction are in a large measure of nonspecific origin, not dependent on the toxicity of the tuberculin alone, as they would be were the reaction of the anaphylactic type. Every general reaction is preceded by a focal one, in which inflammation and consequent absorption occur in a region containing the products of disintegration of body tissue, that is, in the tubercle. These disintegrated proteins, like partly digested proteins from any source, are toxic. Tuberculin may thus be looked upon as the indirect cause of the profound toxemia of the general tuberculin reaction. We are accustomed to think of the response to tuberculin in terms of the well-known skin reaction. The skin is by no means the only tissue sensitized in the tuberculous animal or man. Probably all cells are made allergic, that is, sensitive to tuberculin. But this susceptibility varies with the nature of cells, connective tissue being the most resistant, whereas nerve cells are among the most susceptible. A tuberculin test is described which utilizes the exquisite sensitiveness of the germ cells of tuberculous guinea pigs to the action of tuberculin. To elicit this test, 0.1 cc. of 10 per cent old tuberculin is inoculated directly into the testicle of a tuberculous pig. This test is more complicated than the skin test, but is believed to be correspondingly more delicate. Convincing chemical evidence for or against the protein nature of the active principle of tuberculin has not yet been obtained. However, by extraction or precipitation, highly active tuberculins have been prepared which fail to give any of the protein reactions. Chemical protein tests, however, are not of great delicacy. In the use of media of known original composition, there is much hope for a more thorough understanding of the metabolism of the tubercle bacillus. Determining the chemical formula of a protein tuberculin would be impossible with present means, in view of the great complexity of proteins, but if the active principle is nonprotein, the actual formula is a goal not beyond reach.—*A Review of Some Recent Studies on the Metabolism of the Tubercle Bacillus and on the Nature of Tuberculin, E. R. Long, Tubercle, December, 1924, vi, 128.*—(*J. S. W.*)

Respiration of Tubercle Bacillus.—Respiration is a fundamental phenomenon of life: it is the one sure sign of intracellular activity, and its absence or cessation is an unerring indication of impaired vitality or death. In the case of a slow-growing microorganism, such as the tubercle bacillus, it is not possible to ascertain that a subculture is alive and multiplying until the mass has perceptibly increased, which occurs usually after the lapse of a week or two. By the manometric method, the viability of the transplant is indicated within a few hours, provided the medium is such as to give a respiratory quotient which is appreciably less than one. By the use of exact methods, the gas changes of a single strain of human tubercle bacillus (H 37) were followed under varied conditions of growth on solid media. The analyses demonstrated that the gas exchange was greatest when the bacillus was grown on glycerol-agar. Also, in order to obtain a rich growth in a single tube, about 100 to 150 cc. of oxygen must be provided. This means a supply of air corresponding roughly to 500 to 700 cc. at 37°C. and 750 mm. barometric pressure. In a closed, ordinary culture tube the oxygen was removed in a few days by the inoculum, and no visible growth resulted. A very slow growth, or none, in tubes closed either in the

flame, or with sealing wax, paraffin, or rubber stoppers means an insufficient supply of O_2. Such methods of sealing tubes are usually employed on the assumptions that there is enough oxygen in the tube, and that any additional needed oxygen can readily enter through such seals, except the flame-seal. The former assumption is incorrect, while the latter rests purely on the element of chance, which at times may be favorable, at other times unfavorable. Consequently, the results may range from no growth to a rich one. When using glycerol-agar as a culture medium, the manometer developed a negative pressure which reached a constant level as soon as the O_2 was entirely consumed. Some of this negative pressure was due to loss of CO_2 by solution in the medium, etc. Rich cultures developed in tubes which were refilled with pure air as often and as soon as the O_2 removal indicated. Thus 5 to 10 refills supplied sufficient O_2 to provide a good growth. It was also found that the volume of growth was strictly proportional to the amount of O_2 consumed, provided the O_2 tension was constant. When such tubes were refilled, so as to contain increasing tensions of O_2, growth became more abundant (increased negative pressures), and the optimal concentration of O_2 was found to be about 40 to 50 per cent. Above that limit growth was less abundant. Growth occurred when the O_2 tension was decreased below that in air. An essential condition for good growth under diminished tension is that the vessel shall contain at least 100 cc. of O_2. Growth continues "until the last atom" of oxygen is consumed. In atmospheres containing 10 to 50 per cent of CO_2 the growth of the tubercle bacillus was not inhibited. In concentrations of 60 per cent or more there was some inhibition, but fair growth was obtained in 90 per cent CO_2 in the presence of the necessary oxygen. Moisture sufficient to wet the surface of the medium was found to be an important factor in securing rich and even growths. The best results, as regards rapidity of growth and richness of culture, were obtained with a meat-extract medium containing 1 per cent agar and 5 per cent glycerol. Moisture can be supplied by a fine jet of steam introduced into the cotton plug. After incubation such tubes were closed with sealing-wax and holed by means of a hot platinum wire. This method of cultivation and steaming is recommended, since in from seven to ten days it gave good growths. The respiratory changes of the tubercle bacillus are quantitatively the same as those of other microörganisms, although the rate of exchange is necessarily slower. Their slow multiplication in the body is explained from the standpoint of growth in diminished O_2 tension. An indefinite supply of O_2 under a tension corresponding to a few millimetres of mercury will probably enable the bacilli to grow, though very slowly. The "rest cure" and rich diet, in checking the progress of the disease, probably act by reducing to a minimum the available O_2 supply in the tissues.—*Microbic Respiration. II. Respiration of the Tubercle Bacillus, F. G. Novy and M. H. Soule, J. Infect. Dis., February, 1925, xxxvi, 169.*—(*J. S. W.*)

Types of Tubercle Bacilli.—In a recent inquiry into the epidemiology of pulmonary tuberculosis in Great Britain Brownlee claims to have succeeded in demonstrating three clear cut types of the disease. These are (1) the "young adult" type, showing a maximum mortality in males between the ages of 20 and 25 years; (2) the "middle age type" which exacts its toll, in males, between the ages of 40 and 45; and (3) the "old age" type which has its maximum mortality in males between the ages of 55 and 65. He found the distribution of these types to be unequal throughout the country. Thus in Shetland, and to a less extent in Ireland, type 1 is prevalent, in London type 2, and in Cornwall type 3. Brownlee offers two possible explanations for the occurrence of these types or groups. The first suggestion is that there are two distinct strains of tubercle bacilli, each having a special age distribution. One of the strains attacks in early manhood and possibly also in old age, the other in childhood and middle life. The second explanation is that "the physiological response to attack by the organisms may be different according to the environment in which the individuals attacked have lived." The first hypothesis presupposed the existence of at least two types (not referring to human or bovine) or groups of tubercle bacilli. A recent investigation by Smith of eleven strains of tubercle bacilli indicates that "groups probably do not exist." Tulloch, Munro, Ross and Cumming, in a more extended investigation involving the isolation and testing against an active immune serum of 100 strains of tubercle bacilli from cases of pulmonary tuberculosis, found no definite existence of "type" or "groups." It would seem, therefore, that the statistical postulate of the existence of two groups of human tubercle bacilli still requires proof, and that the present bacteriological evidence is against the idea. The second explanation advanced by Brownlee is, in view of the above, better suited to explain the facts of the case. In brief, it is that the immunity of the inhabitant of the "tuberculous" environment depends upon an active immunity

which has developed as a result of contact with the bacillus from birth (tuberculization). On the other hand, tuberculosis is rare in isolated communities, due to the rarity of the tubercle bacillus, but should an inhabitant from such an area enter an environment in which tuberculosis is common he exhibits a greater susceptibility to the disease than the native inhabitant. Moreover, the disease in such a subject tends to be generalized and rapid in its course. The difference in environment, the relative degree of intercommunication and the frequency of tubercle contamination largely determine the statistical type developing.—*Types of Tubercle Bacilli, G. R. Ross, Lancet, February 14, 1925, ccviii, 330.*—*(J. S. W.)*

Growth of Tubercle Bacilli in Liquid Media.—Under ordinary cultural conditions the tubercle bacillus is strictly aerobic, growing only on the surface of the media, exposed to the air; its development in the depths requires media, such as Besredka's; also Arloing and Courmont have obtained homogeneous cultures producing a uniform turbidity in broth, in which both virulence and acid-fastness were greatly modified. These aerobic conditions, however, do not parallel those under which the tubercle bacillus lives in the body, especially in avascular formations. Here the tubercle bacillus is never, like the diphtheria bacillus, a surface parasite, but produces its characteristic pathological changes within the tissues. Growth in the depths of media is obtainable either by reinoculating ordinary culture liquids with a surface colony, or, better, by direct culture of serous exudates and tuberculous organs. For the first method glycerinated broth or peptone water (1 to 2 per cent peptone, 2 to 5 per cent glycerine) are used in small tubes. The tubes are shaken after inoculation to cause the fragments to settle. If a little piece of cotton or cotton-wool is immersed, the growing colonies will adhere to it. They appear after three or four weeks, in the form of gray or white granules, which become arborescent. When the colonies are numerous they form a sort of fine dust. The biliated bacilli of Calmette form similar colonies. Growth is always slow and less abundant than in superficial cultures. In the immersed colonies the bacilli keep their acid-fastness and habitual characteristics. In the sucrated media they are shorter and fewer than in the glycerinated; in the albuminous media they are often granular, and sometimes very long. Under liquid petrolatum their vitality and virulence persist for a very long time, as much as two years. These colonies produce no obvious change in the culture media and do not give off the characteristic odor of surface cultures. The filtered liquid contains only minimal quantities of tuberculin. Deep cultures produced by direct inoculation of tuberculous organs or exudates. Prior to the popularization of Petroff's medium, peptonated and glycerinated potato medium was most used generally, and the first colonies to appear were in the depths. If the glycerine is reduced and the salt eliminated and the medium poured into tubes, white granular colonies will appear after three or four weeks' incubation. A slight amount of acidity is desirable, and a small amount of dilute acid or an acid salt may be added before incubation. Culture of recent clear effusions, especially those of artificial pneumothorax, yields almost constant results if one-twentieth volume of 0.1 per cent acid potassium phosphate is added to the medium. Pleural fluids themselves are somewhat acid to phenolphthalein, especially longstanding effusions, due to the presence of carbon dioxide, which diffuses or is transformed into carbonates or bicarbonates on exposure to air. Boiling also causes them to lose their acidity, while covering with liquid petrolatum preserves it. Guinea-pig inoculation with the liquid media on which the bacilli have grown causes a local painful edema probably due to the acid phosphate; later tuberculous lesions appear. Similar cultures may be obtained with the blood and organs of tuberculous guinea pigs, but attempts to cultivate the blood of phthisical patients have thus far been unsuccessful even during acute febrile exacerbations. The following conclusions are reached: Tubercle bacilli from animal sources, inseminated on liquid media, tend first to form minute granular colonies on the fluid, the surface film being a later development. The vigor of the bacilli, however, appears to depend on the aeration of the medium. This may serve to explain the abundant proliferation of the bacillus in young, active, highly vascular tissues on the animal, and its disappearance in old, avascular, encysted lesions.—*Sur la croissance du bacille tuberculeux dans les milieux liquides, E. Buc, Rev. d. l. Tuberc., August, 1924, v, 520.*—*(A. P.)*

Bacteriolysis of Tubercle Bacilli in Vivo.—Previous results obtained by the authors on the lysis of tubercle bacilli *in vitro* by lipoidal substances were repeated *in vivo*. All degrees of degeneration of tubercle bacilli, from loss of acid-fastness to complete dissolution, were obtained in peritoneal exudates. Lecithin, liver oil, olive oil and green soap were used. Lecithin and liver oil were most actively bacteriolytic, while olive oil was much less effective and green

soap practically inactive. The bacteriolytic effect of the first two named was observed (1) when the lipoidal substance was injected first into the peritoneal cavity and followed two days later by virulent tubercle bacilli; (2) when lipoidal substance and bacilli were injected simultaneously after standing in the mixed state for two days at 37°; and (3) when the mixture was incubated 80 days before injection. The bacteriolytic action prevented the development of tuberculosis in guinea pigs. In one case lipoid-fast bacilli were found, which resisted the action of the lipoids and also caused tuberculosis in guinea pigs after two days' action of lecithin. A lymphocytosis developed regularly in all guinea pigs with tuberculosis, but it was fully as marked in the tuberculous controls without lipoid treatment as in the treated animals. As the controls regularly developed generalized tuberculosis the lymphocytosis played no rôle in immunity, as compared with the direct action of the lipoids. Various types of degeneration were observed in the leucocytes of tuberculous guinea pigs.—*Ueber die Bakteriolyse der Tuberkelbazillen in vivo (Eine experimentelle Studie), M. Isabolinsky and W. Gitowitsch, Ztschr. f. Immunitätsforsch. u. exper. Therap., December 10, 1924, xli, 497* —*(E. R. L.)*

Autolyzed Tubercle Bacilli.—In a study of enzymes the question arose whether any specific ferments could be demonstrated in tubercle bacilli, which are rich in higher fats and waxy substances. The problem was to see whether any lipase could be demonstrated in a mass of tubercle bacilli grown on suitable solid media, and, if so, what changes it would bring about on the bacillus itself. With the use of methyl and ethyl butyrate as substrates, lipase was readily demonstrated in autolyzing tubercle bacilli. After a certain period a small amount of protease could also be detected. When treated with petroleum ether such a digest yields three separate layers, of which the upper two are most important. 1. The uppermost layer is light amber-colored, and consists mainly of the fat solvent plus the fatty and waxy components of the tubercle bacilli. A neutralized solution of the above was found to have no antigenic powers. 2. The middle layer forms a soft whitish cake and consists of agglutinated tubercle bacilli, most of which are non-acid-fast. Repeated washing of the mass after drying with fat solvents yields a purified product which is finally powdered, weighed, and suspended in physiological salt solution in definite strength. This fraction was found to possess definite but weak antigenic powers when used in the tuberculosis complement-fixation test. On inoculation into guinea pigs it produced definite antibodies, and these treated guinea pigs, when infected with live virulent tubercle bacilli, showed also a definite immunity. This antigen was then used in lymphatic and pulmonary tuberculosis in man. The lymphatic cases showed definite improvement provided caseation and softening had not already occurred. In proper dosage this material produces, occasionally, a small edematous swelling locally, which subsides in two or three days. The general reaction consists of a rise of temperature one to two degrees above the usual during the first twenty-four hours. This drops to normal in two or three days. A course of at least 12 injections given weekly seems to be requisite for a definite improvement.—*Some Products of Autolysed Tubercle Bacillary Cultures with Special Reference to Their Antigenic and Curative Value in Tuberculous Infections, R. Row, Brit. M. J., December 13, 1924, no. 3337, 1110.—(J. S. W.)*

Properties of Defatted Tubercle Bacilli.—To eliminate the fatty waxen substances in tubercle bacilli a method, found useful in the purification of smallpox vaccine, was adopted. Vapors of ether and other fat-dissolving liquids possess a far greater dissolving power than the liquids themselves, while the albumin is left intact. Treating an emulsion of tubercle bacilli energetically with vapors of ether, it was found that the bacilli were killed in ten minutes. On continuing the process the bacilli began to lose their acid-resistance, and the emulsion settled in three layers. The bottom layer contained unaltered acid-fast bacilli, the middle layer partly defatted bacilli, and the top layer a thick stratum of fatty cream. It is stated that defatting did not cause the bacillus to lose its biological properties. Such bacilli are specifically agglutinated by serum of tuberculous persons, but not by that of healthy people. They can be used as an antigen in the complement-fixation test. When injected into animals, agglutinins and other immune bodies are formed. When administered to tuberculous animals or persons the defatted bacilli seem to influence the course of the infection favorably. A correlation of the work with defatted bacilli is hoped for.—*New Ways for Research Work on Tuberculosis, W. Fornet, Med, J. & Rec., January 21, 1925, cxxi, 82.—(J. B. A.)*

Migration of Tubercle Bacilli in Lungs.—One phase of chronic progressive, pulmonary tuberculosis which has been especially attractive to clinical thought is the

apparent migration of the tubercle bacilli from the primary lesion to other portions of the same or the opposite lung. This apparent migration is probably best observed, in a clinical way, by a study of stereoroentgenograms taken at regular intervals in those cases revealing a steady progress of the pumonary process. During the clinical and laboratory study of these cases the sputum should be proved to be bacilli-free, thereby excuding the possibility of aspirated secondary lesions confusing the situation. The clinical and stereoroentgenographic observation of the development of multiple lesions throughout the one or other lung would appear convincing as to the migration of the bacilli from the primary lesion to the various portions of either lung. From the clinical point of view, the migration of the bacilli seems certain; from the anatomical aspect impossible because of the very structure of the pulmonary lymphatics, which heretofore were considered the only pathways open to the migrating bacilli. The presence of valves in the lymph vessels, as proved by Miller, prevents the entrance into the lung of any substances by this route. An investigation was undertaken to determine the probability of material passing from the mediastinum into the substance of the lungs, and the probability of the same kind of material passing from the pleural surface into the lung substance. The primary consideration was not the pathways or means taken by the materials in passing into the lung substance, but the question of the existence of such a passage. Guinea pigs, rabbits, and sheep were used in the investigation. Guinea pigs and rabbits are known to have very thin pleurae and poorly developed septa of the secondary lobules. Sheep, on the other hand, have a thick pleura and well-developed septa, very similar to those found in the human lung. The first set of investigations was to determine the transmissibility of material from the mediastinum into the lung substance. Solutions of india-ink were injected at weekly intervals into the mediastina of the animals. At autopsy these animals showed collections of pigments within the pareital pleura on each side, but notably none beneath the diaphragmatic pleura and none in the liver or spleen. In a second investigation another series of guinea pigs, rabbits and sheep was taken, and the same quantity of material, with the same time intervals as used in the mediastinum cases, was again employed, the site of injection in these cases being the right pleural cavity; due precaution was taken that the lung tissue was not injured. At autopsy the pigment was found scattered throughout each lung, the quantity in the left being as great as that in the right. The distribution was similar in all respects to that found in mediastinum cases. These experiments demonstrate beyond question that rather coarse material, such as an aqueous suspension of charcoal, can through some pathways migrate from one portion of the thoracic cavity to another portion and throughout the respiratory tissues. The mechanism of this migration depends probably more upon the physiology of the pulmonary respiration, with the almost constant movement of the intrapulmonary fluids, than upon phagocytosis or lymph flow as it was formerly conceived.—*The Pathways of the Mediastinum, the Lungs, and the Pleura, J. C. Lyter, Am. J. M. Sc., December, 1924, clxviii, 882.*—(*B. T. McM.*)

Disappearance of Saprophytic Acid-Fast Bacilli from Blood.—Timothy bacilli injected intravenously in rabbits disappear rapidly from the blood-stream. When one-fifth of an agar culture is injected no bacilli can be found in the blood after 48 hours. When 3 agar cultures are injected none can be found after 120 hours.—*Ueber das Verschwinden von säurefesten Bazillen aus der Blutbahn, T. Koizumi, Ztschr. f. Immunitätsforsch. u. exper. Therap., December 10, 1924, xli, 504.*—(*E. R. L.*)

Attempt to Differentiate Acid-Fast Saprophytes from Tubercle Bacilli by Antiformin.—Acid-fast bacilli (tubercle bacilli and saprophytes) were suspended in sterile distilled water, to which was added an equal volume of 40 per cent antiformin, after which they were washed and studied microscopically in Ziehl-Neelsen smears (modified according to Günther). Of the saprophytic cultures 6 proved of low resistance to antiformin, being dissolved in 20 to 30 minutes. The Friedmann strain dissolved in 20 per cent antiformin after 4 days at room temperature and a subsequent 5 days at 37°. Three types of tubercle bacilli and a culture obtained from tap water (saprophytic) were not completely dissolved after 16 days' exposure to 20 per cent antiformin at room temperature and (after renewing the solution) an additional 16 days at 37°. Relatively, the human tubercle bacillus was most affected, then the water bacillus, the bovine bacillus and finally the avian bacillus. Attempts to use higher temperatures for differentiating acid-fast saprophytes and tubercle bacilli were not successful. At 80° and 100° the water bacillus proved as strongly antiformin-resistant as the avian tubercle and human tubercle bacilli, and the bovine bacillus was a little less resistant to 20 per cent antiformin. It is not

possible by antiformin to differentiate the saprophytes from tubercle bacilli.—*Zur Trennung der säurefesten Saprophyten von den Tuberkelbazillen mittel, Antiformin, H. Hörig, Dissertation, Leipzig, 1923, Abstract from Centralbl. f. d. ges Tuberk.-Forsch., July, 1924, xxii, 263.*—(*H. J. C.*)

Differentiation of Acid-Fast Saprophytes from Tubercle Bacilli by Preiss's Method.—Using the Preiss method for staining tubercle bacilli with carbol-fuchsin and decolorizing by boiling, the author verified Preiss's observations on the resistance of the tubercle bacillus to boiling water. The human bacillus revealed a resistance to boiling of at least 6 minutes for sputum and over 20 minutes for cultures, the bovine bacillus in the majority of cases had a resistance of 10 minutes with smears from organs to 25 minutes with cultures, and the avian bacillus in the majority of cases had only a resistance of 2 minutes. With one exception the acid-fast saprophytes, in agreement with Preiss's findings, were decolorized after 2 minutes in boiling water. The exception occurred with an acid-fast saprophyte obtained from tap water which was found as two different varieties, and proved resistant to 7 and 30 minutes of boiling. In pure cultures the latter was resistant to boiling for 10 minutes. Because of the danger of contamination with this organism in animal excretion, it is believed that the Preiss method for differentiating tubercle bacilli and saprophytes in the examination of secretions and excretions is of no value for differential purposes.—*Zur Trennung säurefesten Saprophyten von Tuberkelbazillen durch das Preissche Kochverfahren, A. Petzsch, Dissertation: Leipzig, 1923, Abstract from Centralbl. f. d. ges. Tuberk.-Forsch., July, 1924, xxii, 264.*—(*H. J. C.*)

Experimental Tubercle-Bacillus Bacillemia in the Guinea Pig.—It was Villemin who first proved the transmissibility of tubercle virus in the blood by inoculating, in 1865, healthy rabbits with the blood of phthisicial patients and tuberculized rabbits, and finding tubercle at autopsy of the animals. The passage of bacilli in the blood explains the mechanism of miliary tuberculosis, fetal tuberculosis and distant bacillary metastases. Pathological anatomy shows us tubercles in the walls of the blood vessels, and the microscope shows the bacilli in infarcts and emboli, but their actual recovery from the blood is much more difficult. The attempts to solve the problem by direct blood culture have entirely failed, while reported direct microscopic positive findings by certain authors have been shown to be vitiated by technical errors, since acid-fast bacilli may occur in the water used for the preparations. The production of experimental tuberculosis by inoculation of the blood into animals is a more certain criterion. Of 1,400 inoculations of the blood of tuberculosis patients, not gravely ill, 250, or about one-sixth, have proved positive, showing that septicemia in tuberculous infection is not rare. The present studies deal with 40 cultures from the blood of tuberculous guinea pigs, using as media glycerinated broth, glycerinated potato water, glycerinated dilute horse serum, and a modified Dorset medium. Five or six drops of blood were aspirated from the heart with a pipette and planted in 10 cc. of the medium. There were 16 animals infected with tuberculous products (pus, sputum, pleural effusion, organ emulsions), and 24 infected with cultures of bacilli. The first group yielded negative results with the blood, but in the second group 12 positive cultures were grown. It was attempted to select races of tubercle bacilli already habituated to liquid media, and to grow in the depths, rather than superficially. For this purpose a rich culture on Dorset's medium was planted abundantly on 4 per cent glycerinated potato water. At the same time fragments of egg-yolk were emulsified near the surface with several drops of water in an inclined position of the tube, which was gently shaken. Each day, during incubation, the tube would be shaken several minutes. This served to produce homogeneous cultures, finely granular or flocculent. These seemed well adapted for inoculation of the experimental animals with the idea of getting the bacilli to grow in the blood. Of the 12 positive cultures 11 were of the human type, 1 bovine. In 5 cases, considered negative, microörganisms were grown, but feeble and atypical, not growing on subculture. They either colored a pale blue with Ziehl-Neelsen stain (5 cases), or presented the granular form described by Much (1 case), or a coccoid form (1 case). In 4 of the so called negative cultures of the first group there were found non-acid-resistant, non-transplantable forms, in one case Much's form, and in one case a streptothrix. Of the typical undoubted positive cultures, all showed typical acid-fast forms on subculture. Young cultures, however, frequently showed mixed red and blue-colored bacilli, the one growing on gelatin in dry, whitish, verrucous colonies, the other moist, grayish, and smooth. The race which had lost its acid-fastness was difficult to preserve and would not grow after two years, in several instances failing to infect guinea pigs. Neither did the acid-fast race preserve its

virulence. The non-acid-fast forms may be either immature or attenuated bacilli; in the latter case their virulence is impaired or lost. Some filamentous faintly-staining forms were grown on horse serum, resembling streptothrix, but always reverting to the acid-fast type on subculture. It thus appears that residence in the blood alters the aspect and attenuates the virulence of the the bacilli. Costantini has made similar observations, and also finds that after a week's residence in the blood the bacillary forms give way to Much's forms. Marmorek has also noted that guinea pigs inoculated with bacilliferous blood contract a tuberculosis which evolves more slowly than in controls inoculated with the same culture. Karwacki has attempted to enhance the virulence of tubercle bacilli by repeated passage through animals, making intraperitoneal injections. After three passages he succeeded in killing a guinea pig in eleven days with 4 cc. of *bacilles-sang*, and found at autopsy a serohemorrhagic exudate rich in bacilli but no macroscopic tubercles. He concluded from this that the animal died of tubercle-bacillus septicemia. On continuing the passage twice more he succeeded in killing one animal in five days, and found only congestive lesions, with a micrococcus on blood culture and a pseudodiphtheritic bacillus on culture from the organs. Another animal, killed after two years, showed no tuberculous lesions. He suggests that the tubercle bacilli were destroyed by bacteriolysis, with the elaboration of toxic protein substances and that as the bacilli increase in virulence they become more susceptible to bacteriolysis. He also believes that the tubercle bacillus may undergo mutations and transformations which end with a coccus or a polymorphous bacillus, which is no longer tuberculogenic. He affirms that a race of homogenized tubercle bacilli, inoculated *en passages* in guinea pigs and isolated from their blood, has provoked an infection without tubercles, that their virulence continually increased, and that finally their acid resistance began to wane and disappeared. This acid-resistance is to be regarded as a protection, while at the same time it checks bacillary activity. Its diminution facilitates multiplication and massive infection, but exposes the bacilli to phagocytosis and cytolysis. Finally the tubercle virus loses its faculty of producing a chronic process, and either provokes an acute fatal septicemia or itself succumbs. *Conclusions:* 1. The ill success of blood cultures in tuberculous septicemias is due to the lack of a suitable medium. If properly carried out, 50 per cent positives are obtainable. 2. Repeated passage through guinea pigs and recovery from their blood result in a type of bacillus which produces septicemia without tubercles. 3. After such repeated passage the bacilli, although increased in virulence, lose their acid-resistance.—*Septicémie à bacilles de Koch dans la tuberculose expérimentale du cobaye, L. Karwacki, Rev. d. l. Tuberc., October, 1924, v, 658.—(A. P.)*

Pathognomonic X-Ray Signs in Early Pulmonary Tuberculosis.—A doubtful or early lesion in the lungs may cast a certain shadow on the X-ray plate. If the plate is taken, the patient then given sufficient tuberculin to produce a focal reaction, and then a second plate taken, the focal reaction is often present on the latter plate. The finding is to be regarded as pathognomonic for tuberculosis, since tuberculin will elicit no reaction in any tissue that is without a focus of tuberculosis.—*Pathognomonic Radiographic Finding in Early Pulmonary Tuberculosis, R. M. Hayes and I. S. Trostler, Radiology, December, 1924, iii, 474.—(H. S. W.)*

Periodic Febrile Exacerbations in Pulmonary Tuberculosis.—Attention is drawn to a particular form of temperature curve, characterized by the appearance of sharp febrile exacerbations at regular intervals, and separated by periods of complete apyrexia. Three typical cases among patients at the Popular Sanatorium of Leysin are cited. The first was a patient with bilateral fibrocaseous tuberculosis with a right-sided cavity. The exacerbations lasted three or four days, and the intervals seventeen to twenty-four days. Of ten exacerbations, five were at equal intervals. During these exacerbations the cough, expectoration and constitutional symptoms were aggravated, but the physical signs were very little altered, never more than transient congestive manifestations being present. In the second patient, a man with chronic bilateral ulcerofibrous disease, there were twelve sudden thermic flare-ups, separated by intervals of 16 to 44 days. Ultimately a characteristic remittent fever developed. The last case, of cavernous type, came to autopsy. He had six febrile exacerbations separated by a seventeen to twenty-day interval. The autopsy findings, although showing a large cavity, failed to explain the exacerbations. *Discussion:* These crises or exacerbations are of sudden appearance and disappearance, and not over a few days' duration. The usual interval between them is 25 to 35 days. They yield to no treatment. Several hypothetical explanations are analyzed as follows: 1. *Active*

evolution of the disease: In such cases the thermic elevations are accompanied or followed by pulmonary signs indicating the appearance of new foci, and the general condition is almost always impaired. Such signs were conspicuously absent in the cases described, and the general condition was not seriously affected. 2. *Intracavitary retention:* It is true that all three patients had cavities, and the sudden increase in expectoration might lead one to suspect a connection. However, the careful daily observation of the amount of expectoration showed that there was no drop prior to the flare-up, such as would occur if drainage were blocked, and the evacuation of sputum was not sudden, as when a cavity is emptied, but the sputum curve closely paralleled that of the temperature. Finally, fluoroscopic examination of one patient showed no change in the appearance of the cavity during or after the crisis. 3. *Miliary dissemination or bacillemic showers:* It is well known that in addition to generalized miliary tuberculosis there are more or less localized regional forms, often curable. In the classical types there are slight dyspnea and cyanosis, a sense of thoracic oppression, rapid pulse, and impairment of the general condition. Auscultation may reveal little, but radiography may show the miliary dissemination very clearly, and occasionally there is evidence of temporary bacillemia. None of the cases here described, however, gave any such proof, nor was the temperature curve comparable to that of miliary dissemination. Still, it must be considered a possibility. 4. *Biology of the bacillus:* The alternating phases of immunity and parasitic activity are well known in the case of malaria, recurrent spirillar fever, and probably amebic dysentery. May there not be a similar cycle in the evolution of the tubercle bacillus in its host? A sudden liberation of endotoxins might account for the sudden fever, emanating from sudden focal congestive recrudescences. This must, however, be regarded at present as pure hypothesis. 5. *Neurovegetative periodicity:* No other evidence of endocrine or neurovegetative disturbance was found in these patients. 6. *Phenomena of alternating immunity:* The mechanism of immunity and sensitiveness is known to be very delicate in the tuberculous. Repeated skin tests were performed on one of the patients, all being identical; on another, there seemed to be a temporary variation. This hypothesis is rather favored by Burnand and Bothézat. According to it, in the undulating or hectic fever there is a sort of rhythmic balance between allergy and anergy, but no opportunity for a sustained immunity to develop because of the severe infection. Here, however, the long intervening period is evidence of a well sustained defense, which, however, is suddenly interrupted, as the foci give out an unusually toxic discharge. There seems to be some presumptive evidence of such focal activity, which eventually may break down the defenses, and a typical undulating fever curve then appears.—*Poussées fébriles brusques et périodiques chez certains tuberculeux pulmonaires du sexe masculin, R. Burnand and M. Bothézat, Rev. d. l. Tuberc., August, 1924, v, 492.*—(*A. P.*)

Fever and Pulmonary Tuberculosis.—Clinicians of an earlier date described the fevers of tuberculosis as remittent, intermittent, or hectic in type. More recently attention has been called to further variations in the type of fever; the fever of overexcretion, the cyclic fever accompanying an extension of the lesion, the undulating type of fever, the periodic fever, etc. A precise description of these various forms is given. The author finds the fever differing in children, according to whether infection is primary or secondary. Up to about two years, infection is usually primary and fever is slight, but with frequently occurrring periods of elevated temperature lasting from four to six days, and of abrupt onset; terminal fever is most often due to tuberculous meningitis or bronchopneumonia. In older children infection is a rekindling of a first infection, or a late primary infection, and fever is seldom lacking. The various types are described. They resemble more and more the fevers of adults, as age increases. The fever of tuberculosis in the adult is studied in the light of the newer knowledge of reinfection as the fever of onset and that of established pulmonary disease. The description includes the fever of cyclic evolutive extension with relatively sudden onset, the general characteristics of fever during the course of extension of disease, the chronic or prolonged defervescence, the undulating type of fever, the hectic type, the inverse type, and the type with periodic sudden rises. A second section of the article is devoted to temperature instability in the tuberculous, including premenstrual hyperthermy. A third section discusses the diagnosis of mild hyperthermies. Different problems present themselves according as one is studying children, or men or women. Possible causes in the child are tuberculosis of the tracheobronchial lymph nodes, digestive autointoxications, hypersensitiveness to certain food-stuffs, particularly carbohydrates, chronic adenitis and cryptogenic infections. In adults a latent slumbering tuberculosis is a very frequent cause, but

other infections must be excluded. Persistent low fevers, difficult to explain, are particularly common in women, a certain number of whom present endocrine disturbances, which determine symptoms very similar to those caused by mild latent infections, especially tuberculosis. After tuberculosis and the various other causes have been eliminated, there still remains a group described by Cawadias under the name of *fièvre sympathique.—Fièvre et tuberculose pulmonaire, F. Bezançon, Ann. de Méd., Decembre, 1924 xvi, 496.—(W. B. S.)*

Superficial Venules in Pulmonary Tuberculosis.—Enlarged superficial venules on the trunk were studied and charted in 250 cases. The groups of venules anteriorly are designated as the *sternocostal* or *costal arch*, and the *diaphragmatic arch*. In the former the apex of the arch is formed by venules over the sternum at the level of the second or third rib or higher, while the limbs of the arch are formed by venules in line with these spreading out on each side. As a rule, only one costal arch is present; sometimes only a fraction of one, and infrequently two, one above the other. The diaphragmatic arch corresponds to the line of attachment of the diaphragm. Posteriorly, the venules are also arranged into two definite groups: (1) around the seventh cervical and first and second thoracic spines (zone of Lombardi); and (2) along the crests of the ilium (cristal line). Venules may be scattered irregularly elsewhere. Frequently also actual varices may be formed between the anterior thoracic veins and the internal mammary, or between the internal mammary, the anterior thoracic veins, and the veins of the upper arm, or between the internal mammary, the upper anterior thoracic veins and the intercostals. These varices are sometimes due to partial obstruction of the subclavicular vein by pleuritic adhesions. An enumeration of the venules found in the cases studied is tabulated. Factors operating in pulmonary tuberculosis, to make the veins of the thoracic wall conspicuous, are thinness and atrophy of the skin, respiratory strain, pressure of intrathoracic masses on blood vessels, and labored action of the right side of the heart. Superficial venules represent collateral circulations, and are produced mainly by obstruction of the azygos part of the superior vena cava system. A clinical study of the various relationships of the venules was made. *Conclusions:* The number of distended venules in the trunk depends on: 1. Age: an increase with advancing years till the atrophy of old age. 2. Duration of disease: increases with duration of disease. 3. Cough: increases with the amount of cough. 4. Fibrosis: increases according to its extent. 5. Anatomical extent of disease: independent of it; no use in prognosis. 6. Locality of disease in lung: independent of it; not a means of localizing the disease at first sight. 7. Not reflex or trophic in cause as is, for example, local muscle change. 8. Definitely associated with pulmonary tuberculosis, and in the main due to obstruction of the azygos veins by enlarged mediastinal lymph nodes and hilum fibrosis (especially in children), although also due to general lung fibrosis and strain on pulmonary and general venous circulation.—*Superficial Venules in Pulmonary Tuberculosis, A. N. Robertson, Tubercle, January, 1925, vi, 165.—(J. B. A.)*

Diagnosis of Pulmonary Tuberculosis.—The characteristic general symptoms of tuberculosis, such as subfebrile temperature, night sweats, clamminess, disturbances of the innervation of the vessels and the heart, anemia, dyspeptic and psychic disturbances, etc., can with certainty be attributed to an active tuberculous lesion only when all or at least the majority of them are coincidently present. The known biological reactions of the present day are not more reliable than these in diagnosis. Especially characteristic for the tuberculous etiology of a questionable focus are the associated râles, which differ from those of a nonspecific catarrh. By no means all localized apical catarrhs are tuberculous. Of practical value in the diagnosis of specific pulmonary disease are the persistence and long duration of physical findings, in other words the difficulty of their being influenced by therapeutic means, while nonspecific catarrhs show marked changes within a short time. Purely tuberculous tissue changes can rapidly increase objectively, but they disappear only slowly; the same is true of syphilis and chronic pneumonia, which are rare conditions. It is recommended that examinations be made at the same time of the day and with the same technique as advised by Ulrici. Difficulties are met with in the diagnosis of complicating nonspecific perifocal catarrhs. They develop in a number of weeks and retrogress, and have the appearance of a rapidly healing tuberculous lesion. A division into four groups is made. In the first group are included the closed cases of pulmonary tuberculosis, with negative or inappreciable objective pulmonary findings, in which there is no association with the bronchi or there is complete fibrosis. The second group includes cases, in which if the lesion has broken through the bronchial tree it is only small. The third group includes the facultative open form of tuberculosis,

with outspoken characteristic pulmonary findings, there being an open ulcerative lesion in the bronchial tree. The fourth group includes the obligate bacillus excretors, with outspoken objective pulmonary findings in which the wall of the lesion is of a neoplastic nature. The anatomical progression of a tuberculous process is unquestionable when, as a result of a nonspecific perifocal catarrh, elastic fibres are found or hemoptysis occurs. Such a perifocal inflammation can also involve the pleura and produce a pleuritis, which is more easily noted than the small and inconveniently located associated pulmonary focus.—*Ueber die Korrelation zwischen tuberkulösem Lungenherd mit allgemeinen und örtlichen klinischen Krankheitsbildern, A. Winkler, Beitr. z. Klin. d. Tuberk., 1923, lvii, 164.*—(*H. J. C.*)

Diagnosis of Apical Bronchiectasis.—In 1910 the author reported a case of bronchiectasis of the right apex not diagnosed in life; the patient died of hemorrhage. At that time no other case was found in the literature. A second case is reported of a 16-year-old girl observed for 1¾ years, and the tentative diagnosis is either bronchiectasis of the left apex or tuberculosis, the physical symptoms of which are almost identical. The X-ray is of no aid. Absence of tubercle bacilli and elastic fibres is of not much value. The negative tuberculin test is, however, significant. Time is also a prime diagnostic aid. It is concluded that bronchiectasis of the apices are clinically almost impossible of diagnosis.—*Beitrag zur Diagnostik von Spitzenbronchiektasien, A. Bauer, Beitr. z. Klin. d. Tuberk., 1923, lvii, 61.*—(*H. J. C.*)

Differentiation of Pneumonokoniosis and Tuberculosis.—The anthracosis and chalicosis of miners can be differentiated by utilizing all the available clinical diagnostic methods. The roentgen picture is especially valuable. Typical for both pneumonokonioses is the almost uniform and symmetrical distribution of the shadows, especially in the mid-parts of the lungs, and this is especially true in chalicosis, which also gives more dense shadows than anthracosis. Coal dust is less dangerous than stone or mineral dust. Chalicosis need not lead to tuberculosis, but if they are associated the prognosis becomes unfavorable. Elevation of temperature strengthens the suspicion of tuberculosis. Apical lesions, roentgenologically, in an otherwise typical pneumonokoniosis plate speak for tuberculosis; otherwise a roentgenological differentiation is impossible.—*Über Pneumonokoniosen bei den Bergarbeitern des rheinischwestfälischen Steinkohlenreviers, Patschkowski, Beitr. z. Klin. d. Tuberk., 1923, lvii, 113.*—(*H. J. C.*)

Percussion of Lungs of Children.—A modified type of percussion is described for examining the chests of very small children. With the usual method of hammer or finger-finger percussion, changes are often missed. In children with tuberculous bronchitic disease, impairment is always noted in the axillae or in the region of the third or fourth rib. In infants the note is always impaired in the left axilla. These changes in the lungs are frequently obscured by percussion before sensitiveness to tuberculin (Pirquet or Mantoux) appears. Ninety per cent of the cases show confirmation of these physical findings by X-ray of the chest. On auscultation there are usually no changes to be elicited over these areas of impairment, but occasionally a diminution of breath sounds is noted.—*Ueber die Perkussion der Lungen bei Kindern, J. S. Arkawin, Deutsche med. Wchnschr., January 30, 1925, li, 192.*—(*H. S. W.*)

Serial X-Rays in Miliary Tuberculosis.—Miliary tubercles cannot be seen in X-ray plates, but the small conglomerate areas of tubercle cast the type shadow seen in miliary disease. In generalized miliary tuberculosis the lungs are studded with minute areas uniformly distributed throughout both organs. Early plates show occasional, very minute infiltrations; these rapidly grow and new ones rapidly come to view. The radiographic evidence of miliary tuberculosis cannot be used to determine activity unless serial plates are taken. Miliary involvement of the lung may exist in the absence of generalized miliary disease and serial radiographs, clinical observation and autopsy examination all point to the fact that such a condition does exist and, further, that it may heal.—*Study of Miliary Tuberculosis by Serial Radiographic Examination; Evidence Indicative of a Chronic Form and Suggestive of a Healed Form, L. R. Sante, Radiology, December, 1924, iii, 457.*—(*H. S. W.*)

X-Ray Examination of Pulmonary Tuberculosis.—The radiologist who interprets chest plates should do so in close relation with the clinician, who knows the history and physical findings of the patient whose plate is under review and should always be keen to see or learn the autopsy results of fatal cases. Otherwise, reading into the interpretation such a statement as that of "activity" or "inactivity" is unjustifiable. One should describe the various densities only, and should avoid arriving at

a diagnosis by other means. He should come to the diagnosis only by what is seen in the plate. If he has conferred with the clinician and pathologist often enough to build up an experience, he can and should give an impression of "active" or "inactive" tuberculosis after he has described the densities. The shadow about a cavity may be dense and fibrotic and represent a satisfactory degree of fibrosis, or the cavity may grow to include an entire lobe, the parietal and visceral pleurae becoming adherent and the space being taken for an area of pneumothorax. "Peribronchial tuberculosis" is an unfortunate term, as it is frequently applied to bronchial thickening radiating out from the hilum and having some other cause. True peribronchial tuberculosis is essentially a tuberculous lymphangitis. Evaluation of root changes in the lungs of children is one of the greatest difficulties in radiological work. Lymph-node disease at the hilum in children may result from any of the childhood infections, and in plates may be identical with the changes set up by tuberculosis in this situation, and clinical findings are essential to a diagnosis. Hilum tuberculosis, when it exists in adults, is most commonly associated with tuberculosis of the abdomen or of bone and is often similar in X-ray appearance to Hodgkin's disease or lymphosarcoma.—*The General Aspect of Tuberculosis as Presented by X-Rays, J. D. MacRae, Radiology, December, 1924, iii, 464.*—(*H. S. W.*)

Thoracoscopy in Pulmonary Diseases.—The thoracoscopic method, improved by Unverricht, is a valuable aid in determining pleural disease, and with it diaphragmatic conditions were also treated. In 4 of 11 cases the intrapleural severance of adhesions made possible a complete collapse. Suitable cases are small in number. Hemorrhage was not encountered. The color of the adhesions is a good index of their vascularity. Thoracoscopy in the presence of a recently initiated pneumothorax is warned against, since the pleura easily tears and an effusion results. Empyema was not noted in any of the 11 cases.—*Die Thorakoskopie als diagnostisches und therapeutisches Hilfsmittel bei Erkrankungen der Brustorgane, A. Gehrcke, Beitr. z. Klin. d. Tuberk., 1923, lvii, 127.*—(*H. J. C.*)

Review of Clinical Laboratory Technique in Tuberculosis.—*Examination of the sputum:* The sputum should be collected in a suitable receptacle containing no liquid, and should preferably be examined the same day. The smears should be made as thin as possible, on clean defatted slides, with a platinum loop. Three stains are especially recommended: Unna's polychrome blue for the cells and amorphous elements, hematoxylin-eosin, particularly for a study of the cells, and orceine-fuchseline, for elastic fibres which appear blue or violet on a rose-colored field. This stain requires six to twelve hours to act. Various forms of elastic fibres may be made out, those from the alveolar walls being finely fibrillar. Among the cellular elements may be mentioned the small rounded alveolar cell, the endothelial macrophage, which often contains granules of dust and hemoglobin, red blood cells, polynuclear neutrophiles and eosinophiles. *Relation between cytology and morphology of sputum and clinical course of disease:* At the onset of the fibrocaseous form the sputum differs little from that of ordinary bronchitis. Later, still preceding the appearance of bacilli, mononuclear and polynuclear cells indicative of an alveolitis appear, and possibly a few red blood cells and a little albumin. Hemoptoic sputum shows, in addition to numerous red blood cells, small round cells and leucocytes, which increase if active evolution occurs. Finally, as softening and ulceration take place, the elastic fibrils, beautifully stained with violet, appear. The acute pneumonic form shows at first a sputum similar to that of ordinary pneumonia, with sero-albuminous exudate, red blood cells, and small endothelial cells. Later appear the leucocytes, the endothelial macrophages, and the elastic tissue, and finally much degenerated debris. The inactive fibrous forms show the sputum of a chronic bronchitis. The presence of many eosinophiles is indicative of asthma. In tuberculosis, elastic fibres appear at about the same time as bacilli.—*Revue critique des techniques expérimentales et cliniques applicables à la tuberculose, A. Bergeron and R. Letulle (suite), Rev. d l. Tuberc., October, 1924, v, 669.*—(*A. P.*)

Complement Fixation in Tuberculosis.—This study was started in 1917 for the purpose of ascertaining the practical value of the complement-fixation reaction in the diagnosis of tuberculosis. The specific character of the antigenic action of the tubercle bacillus has been extensively studied. Although a large number of reactions has been reported in supposedly normal or nontuberculous individuals, improved technique in the hands of more recent workers has so greatly reduced the number of these reactions that it is now difficult to exclude the possibility of the reaction being due to some obscure foci of infection. The reactions which have been obtained with syphilitic serums have been attributed to the lipoids in the

antigens of the tubercle bacillus. They have been most marked with antigens prepared from tuberculous tissues or containing lipoids derived from the culture medium upon which the tubercle bacilli were grown. In the standardization of the test an important feature of the present study was the preparation of immune serum undertaken for the purpose of obtaining a standard for comparison of the activity of different antigenic preparations and for use in the development of an accurately controlled technique. For this purpose guinea pigs, rabbits and horses were inoculated with living or dead bacilli. Horses which received large doses of living bacilli intravenously developed high titre sera within a short period after inocularion. Sufficient serum to serve as a standard throughout the work was obtained for each of the three strains of tubercle bacilli (virulent human and bovine and avirulent human), from single bleedings of highly immunized horses. The immune serum gave cross-fixation with the antigens prepared from homologous and heterologous strains, although fixation was obtained in higher dilution with the homologous antigen. A study of the antigenic properties of fractional extracts of the tubercle bacillus indicated that the antigenic properties are associated with the acetone-insoluble lipoids. The bacterial protein, in association with the lipoids, may be a factor, directly or indirectly, in the antigenic activities. The antigen found most satisfactory was a boiled distilled water extract, freed from bacilli by centrifugating or by filtration through paper, and dialyzed for five days in sterile, neutral distilled water. This retained its titre for months even when repeatedly heated at 56°C. for sterilization. Antigens of this type were not anticomplementary, and gave specific fixation with the standard immune serum up to 1:200. A sodium-hydroxide-extract antigen and a broth-filtrate concentrated antigen were also used in the tests, and occasionally saline extracts of live bacilli, an antigen precipitated by alcohol from broth culture filtrate, and a dialyzed culture filtrate antigen. The concentration of antigenic units in an antigen was found not to be a measure of its sensitivity in tests. This is illustrated by the increased sensitivity of the boiled aqueous extract antigens, especially after dialysis, and of some of the culture filtrates, in the tests of human tuberculous sera, although these antigens contained fewer antigenic units per test dose than the highly concentrated lipoid antigens which were much less sensitive. Antigens possessing high lipoid content were found to give a considerable number of reactions with four-plus Wassermann sera. Removal of the acetone-soluble material from these preparations, however, eliminated these nonspecific reactions to a large extent. In the test, as finally determined, three quantities each of serum and complement with the optimal fixing amount of antigen were used. The dialyzed aqueous extract antigen was used, diluted 1–15, the sodium-hydroxide extract 1–150, and the broth filtrate concentrated 1–200, the dose employed being 0.1 cc. The largest quantity of serum, 0.05 cc., which is not ordinarily anticomplementary with two units of complement, was selected, together with 0.02 and 0.01 cc. Then, by using one, one and one-half and two hemolytic units of complement, as determined by titration in the presence of antigen, an improved multiple serum-complement titration was obtained in the test, which would not only detect any reaction which might be lost in a test with single serum and complement quantities, but would insure the optimal quantitative relations between antigen, serum and complement. The test also included serum controls of the larger quantity of serum, and each of the three complement quantities and of the two smaller quantities of serum with the one unit quantity of complement. Two antigen controls are used, consisting of the test dose of antigen with one, and one and a half units of complement, respectively. Buffered physiological salt solution was employed with a pH value of 7.6, and the aqueous dialyzed antigens were made isotonic with NaCl and also adjusted to pH 7.6. For complement, pooled guinea-pig serum, free from natural amboceptor, was used. The cell suspension consisted of a 5 per cent sheep-cell suspension, diluted with antisheep amboceptor in such a manner that 0.2 cc. of the resulting suspension contained 0.1 cc. of the cell suspension and two units of amboceptor. The serum to be tested was inactivated at 56°C. for one-half hour in the case of human serum, and for one hour at 58°C. in the case of bovine serum. A rather complicated method for reporting the amount of fixation was employed, in which the value of the reaction for each quantity of complement was obtained by adding the reaction obtained with this quantity of complement and each of the respective quantities of serum used. Finally, the complete test was reported as the total percentage of fixation found with all three quantities of complement. Slight nonspecific reactions were subtracted from the result. The following table indicates how these results are recorded:

275 to 300 per cent: nearly complete fixation
172 to 275 per cent: marked fixation

80 to 175 per cent: partial fixation
30 to 80 per cent: slight fixation
8.33 to 30 per cent: very slight fixation

The study of the practical application of the test to the diagnosis of tuberculosis was made with two groups of cases; one at the Albany City Hospital and Tuberculosis Camp; the other at Bellevue Hospital in New York City. It covered a period of two years. After comparing the results obtained in the tuberculous and nontuberculous series, and especially after a study of border-line reactions, the results indicated that a reaction of fixation classified as "slight" or better, with at least one of the three tubercle antigens, could be interpreted as the specific reaction of an active process, but it was necessary to exclude from this category cases which also react in the Wassermann test, on account of the possibility of cross-fixation. This is especially true in those cases of syphilis, which reacted with the lipoidal antigens and failed to react with the aqueous extract. The Albany series comprised 181 cases of which 110 were listed as nontuberculous and 71 were diagnosed as tuberculous. Of the latter, 55 were considered active cases, 6 inactive, and in 10 the diagnosis might be considered doubtful. Ninety-eight of the 110 controls failed to react with any one of the three antigens. Of those reacting, in one case in which it was well marked a review of the history suggested tuberculosis, and three other cases, less marked, gave a family history of tuberculosis: There was also one case of syphilis among these reactors in the nontuberculous group. Twenty-one of the 71 cases diagnosed as tuberculosis failed to react with any one of the three antigens. Five of the 6 inactive cases, and 8 of the 55 active cases, failed to react. The diagnosis of 10 of these cases listed as tuberculosis was considered doubtful. Two of these reacted. The Bellevue series comprised 393 cases: 293 were considered nontuberculous controls and 100 were diagnosed as tuberculosis. Of the 293 controls, 251 failed to react with any one of the three antigens. Forty-two reacted with one or more of the antigens in varying degree. Of the 100 cases diagnosed as tuberculosis, 9 failed to react. By elimination of nonproved cases from the latter group, there remained 4 outstanding active cases of tuberculosis which failed to react, although in only 3 of these were tubercle bacilli demonstrated. The results obtained in the Bellevue series are thus similar to those of the Albany series, save that there is a smaller number of cases of doubtful diagnosis and the results are more definite. The number of cases studied is not sufficient to afford a basis for reliable statistics, especially since the clinical diagnosis may be questioned in a few instances. The control series of nontuberculous cases, however, affords a very fair basis for comparison although the diagnosis in some of these cases is also open to question. Nevertheless, the large number of reactors obtained with the serum of cases of pulmonary tuberculosis, approximately from 85 to 95 per cent in the Albany and Bellevue series, and the comparatively few reactions that occurred with nontuberculous sera, not only demonstrates the practical value of the test as an aid for diagnosis, when interpreted in the light of careful clinical observation, but also suggests the possibility of prognostic significance as experience accumulates and is correlated with the bedside observation. The practical test should be an accurate titration of the activity of the patient's serum. Cross-fixation must be considered in the interpretation of results in cases of syphilis. It is apparent that further standardization of the antigens, and possibly also some preliminary treatment of the patient's serum, will be necessary if the border-line reactions are to be differentiated. The article includes a summary of the findings of other observers and an appendix of nearly 100 pages, in which all reactions obtained in tuberculous and nontuberculous cases are carefully tabulated.—*A Study of the Complement Fixation Reaction in Tuberculosis, A. Wadsworth, F. Maltaner and Elizabeth Maltaner, J. Immunol., January, 1925, x, 241.*—(*J. S. W.*)

Complement-Fixation in Tuberculosis.—The authors prepared the antigens of Besredka, and of Nègre and Boquet, and used them on 445 sera. Four-day Besredka cultures were too poorly grown, so eight-day cultures were used. The results with both antigens were identical. Of 29 cases of incipient tuberculosis without bacilli in the sputum 22 were positive and 2 questionable; of 23 cases of bronchial lymph-node tuberculosis 20 were positive and 1 questionable; of 266 definite cases of tuberculosis in various stages 246 were positive and 6 questionable; of 52 recovered cases 12 were positive and 2 questionable. Six cases of surgical tuberculosis and 4 cases of tuberculosis of the eyes reacted positively. Of 60 healthy individuals one was positive, while of 5 cases suffering from other diseases, 1 diphtheria case was positive. Wassermann-positive sera reacted positively in a higher percentage than Besredka found to be the case. It is concluded that the complement-fixation test is valuable for the diagnosis of active cases of tuberculosis of all types and stages. —*Serodiagnostik der aktiven Tuberkulose*

mittels Komplementbindung mit den Antigenen Besredkas sowie von Nègre und Boquet, A. N. Ginsburg and W. T. Schuwalow, Centralbl. f. Bakt., Abt. I., Orig., 1924, xcl, 363.—(H. J. C.)

Serum Diagnosis of Tuberculosis.—The method of Besredka was found most useful in diagnosing tuberculosis by complement fixation. The antigen was prepared by the following slight modification of Besredka's procedure: Normal sodium-hydrate solution was added to a ten per cent solution of egg-yolk in distilled water to the point of complete clearing, and then normal hydrochloric acid was added to neutrality. If this caused clouding, as it did in a certain number of preparations, sodium hydrate was cautiously added until the mixture just cleared. Distilled water was then added until the original egg-yolk was diluted twenty times. This preparation was sterilized 20 minutes at 110°, cooled, and inoculated with tubercle bacilli from solid media. After growth the cultures were autoclaved and shaken thoroughly with glass beads in small flasks. One-month cultures were found to furnish the best antigen. Young cultures were not suitable, probably because of the poor development of lipoids and products of metabolism. In 75 cases of tuberculosis 56 positive reactions were obtained, including 23 in 27 first stage cases, 18 in 22 second stage, and 6 in 9 third stage. In 17 cases of suspected tuberculosis 8 positive reactions were secured. Eight positive reactions occurred in 40 cases of syphilis. No reactions occurred with the sera of 35 normal persons. The precipitation reaction of Bonacorsi was found to be nonspecific for the diagnosis of tuberculosis, and of no clinical value. Inconclusive results were obtained with the agglutination reaction of Fornet. The authors believe that this method will be of value when technical difficulties in the preparation of the antigen have been overcome.—*Zur Serodiagnostik der Tuberkulose (Komplementbindung, Präzipitation und Agglutination), M. Isabolinsky and W. Gitowitsch, Ztschr. f. Immunitätsforsch. u. exper. Therap., November 25, 1924, xli, 385.—(E. R. L.)*

Staining Tubercle Bacilli in Sputum.—In two cases of pulmonary tuberculosis negative sputum findings were reported with the Ziehl-Neelsen method of staining, but bacilli were promptly demonstrated by using the Schulte-Tigges method. Therefore, the latter should be insisted upon in examining sputum of suspected cases. The technique is given.—*An Aid to Early Diagnosis of Pulmonary Tuberculosis, A. H. Werner, Med. J. & Rec., January 21, 1925, cxxi, 84.—(J. B. A.)*

Konrich's Stain for Tubercle Bacilli.—A drawback to the valuable Konrich method for staining tubercle bacilli is the instability of the sodium-sulphite solution used for decolorizing. A few recommendations are given, according to which the reducing properties of the sulphate solution can be preserved for a longer time. The solution is brought close to the litmus neutral point, pure sodium sulphite only being used, and kept in well stoppered bottles. The desiccated sodium sulphite is preferred because it keeps better, and the solution made from it is twice as strong as when prepared from the crystalline sulphite and a small amount of hydrochinon (0.5 to 1000 cc. sulphite solution). Solutions thus preserved keep for weeks.—*Zur Färbung der Tuberkelbacillen nach Konrich, K. Laubenheimer, Zentralbl. f. Bakteriol., Abt. I., Orig., 1924, xcl, 78.—(H. J. C.)*

Tubercle Bacilli in Urine.—A method for directly demonstrating tubercle bacilli in small amounts of urine, such as specimens obtained by ureteral catheterization, is described. This method is based on the principle that, by diluting the urine with sterile water, the specific gravity of the solution becomes less than that of the bacilli, with the result that the latter are more readily brought down by centrifugation. Removal of pus and detritus further aids. This may be accomplished as follows: A tube of urine is centrifugated at low speed for two or three minutes, thereby removing the bulk of the pus and detritus. One-half of the supernatant cloudy fluid, containing a few pus cells and the bacilli, is poured off into another tube, and an equal amount of sterile water is added. This second tube is centrifugated at highest speed for from fifteen to thirty minutes. The contents of several tubes may be concentrated if desired, the smear being made from the sediment obtained. Another method is to add equal parts of 95 per cent alcohol and distilled water instead of water alone. This mixture is centrifugated at highest speed for forty-five minutes until clear, and a smear is made from the sediment obtained. The Ziehl-Neelsen stain is employed. A more delicate stain is obtained if a steam-bath is used rather than heating the smear with the direct flame. Twenty minutes' steaming suffices. Destaining is accomplished with 30 per cent nitric acid, followed by alcohol (Czaplewski's solution), or by 20 per cent sulphuric acid. Methylene blue is the counterstain. The dangers of error in diagnosis are the same as

with other methods of staining tubercle bacilli in the urine. The smegma bacillus is the chief offender. It is rarely, if ever, present in bladder urine, except as an occasional contamination. It does not invade the renal pelvis. Centrifuge tubes may be cleaned by any method that will ensure the absence of acid-fast bacilli. Using the first of the above methods, tubercle bacilli were found in the urine of 50 cases out of 84 recorded as having renal tuberculosis. With the alcohol method it is believed that the results will be even better.—*A Method of Demonstrating Tubercle Bacilli in the Urine, S. G. Jones, J. Am. M. Ass., December 13, 1924, lxxxiii, 1917.—(J. S. W.)*

Wildbolz Auto-Urine Test.—At the Surgical Charity Clinic of Berlin 60 cases were examined according to Wildbolz's directions; of 24 definite surgical tuberculosis cases 18, or 75 per cent, were positive, and of 36 nontuberculous cases 20, or 55.6 per cent, were positive. The Pirquet reaction resulted positively in 20 of 24, or 83.3 per cent, of definite surgical tuberculosis; and of 36 nontuberculous cases 33, or 91.7 per cent, were positive. With the exception of one 15-year-old case all were from 20 to 65 years of age. Among the definite tuberculosis cases with negative and questionable Pirquet reactions none were cachectic. The positive reactions were visible within 24 hours. The Pirquet reaction is worthless for the diagnosis of surgical tuberculosis in adults.—*Uber die Bedeutung der Eigenharnreaktion nach Wildbolz und der von Pirquetschen Tuberkulinreaktion für die Diagnose der chirurgischen Tuberkulose, H. Landau, Arch. f. Klin. Chir., 1924, cxxix, 636.—(H. J. C.)*

Toenniessen's Tuberculoprotein in Diagnosis—No harmful effects were ever noted from the diagnostic use of *Tuberculoprotein Toenniessen* in 300 cases at the Surgical University Clinic of Erlangen. The reaction should be excluded from all cases suspected of having an active lung process and tuberculous laryngitis or meningitis or caries of the upper cervical vertebrae. The double injection, according to Toenniessen's scheme in surgical tuberculosis, is not advised. When the lungs are free from tuberculosis clinically, the temperature is not elevated, and resistance is good, 0.3 mgm. is given subcutaneously; with subfebrile temperatures, 0.15 mgm. When the lungs are "suspicious," in the absence of fever, 0.1 mgm. is given, and with subfebrile temperature 0.05 mgm.; in spondylitis cases the dose can be still further reduced. Injections are best given early in the morning, so that reactions will not occur during the night. Reactions usually occur on the first day, rarely on the second day. The temperature can be high, 41 to 42°C. A temperature increase of less than 0.6° is considered negative.—*Grundsätzliche Fragen der biologischen Tuberkulosediagnostik. Erfahrungen mit dem Tuberkuloprotein Toennissen, H. Friedrich, Deutsche Ztschr. f. Chir., 1924, clxxxv, 93.—(H. J. C.)*

Diazo Reaction in Progressive Pulmonary Tuberculosis.—Of 51 patients dying of pulmonary tuberculosis, 14 gave a single, in most cases only slight, positive diazo reaction. Of 209 that remained alive with severe pulmonary tuberculosis the reaction was constant five times, and 6 times positive only once or twice. In all the remaining cases, including those with leptomeningitis and miliary tuberculosis, the reaction was negative. It is concluded, therefore, that the Diazo reaction in pulmonary tuberculosis is of no diagnostic or prognostic value.—*Kurze Mitteilung über den Wert der Diazoreaktion bei progedienten Fällen von Lungentuberkulose, H. Stubbe, Beitr. z. Klin. d. Tuberk., 1923, lvii, 261.—(H. J. C.)*

Biological Diagnosis of Tuberculosis.—Characteristic changes occur in the white-cell blood picture following the injection of *Tebeprotein Toenniessen.* Leucocytosis, lymphocytic disturbance and neutrophilia are observed. In a group of cases this change in the blood picture occurred without temperature disturbance or focal reaction, although in a number of cases it accompanied clinical reaction. In another group of cases, in which tuberculosis could not be detected by other means, clinical reaction accompanied by the characteristic blood picture developed. The white-cell change is a valuable aid in the diagnosis of tuberculosis.—*Ein Beitrag zur biologischen Diagnostik der Tuberkulose, H. Seidl, München. med. Wchnschr., September 26, 1924, lxxi, 1355.—(E. R. L.)*

Flocculation of Blood Plasma and Red-Cell Sedimentation Test.—The sedimentation rate and the flocculation reaction of the blood plasma, after the addition of salt solution, were tested on 500 children with tuberculosis of all forms and on 150 female adults, using the technique of Frisch and Starlinger. The flocculation test, as a whole, runs parallel with the sedimentation reaction, even though the latter is more sensitive; yet it can well be confirmed by the flocculation test. In clinically hopeless tuberculosis

of children flocculation was usually persistently increased and in clinically active tuberculosis it was always markedly increased while in clinically inactive tuberculosis it was normal or only slightly increased. Tuberculin injections do not appreciably affect the sedimentation or the flocculation reaction; a differentiation of active from inactive cases cannot be made. There is no difference between the flocculation reaction in children and in female adults.—*Über eine Flockungsreaktion des Blutplasmas und ihr Verhältnis zur Senkungsgeschwindigkeit der Erythrocyten, L. Weise, Beitr. z. Klin. d. Tuberk., 1924, lvii, 367.*—(*H. J. C.*)

Red-Cell Sedimentation Test after Tuberculin Injections.—No specific influence was exerted upon the sedimentation rate of the erythrocytes by injections of old tuberculin. A "subthreshold" injection of old tuberculin did not change the erythrocyte sedimentation by 3 mm. regularly in active tubeculosis. The distinguishing of an active from an inactive case of tuberculosis was not possible by means of the Gräfe and Reinwein method.—*Besitzen wir in der Kombination von Erythrocyten-Senkungsgeschwindigkeit und Injektion von Alttuberkulin nach Grafe und Reinwein eine klinisch brauchbare Tuberkulosereaktion? K. Brünecke, Beitr. z. Klin. d. Tuberk., 1923, lvii, 154.*—(*H. J. C.*)

Red-Cell Sedimentation Test.—In bone and joint tuberculosis increased values in the sedimentation rate, when other inflammatory conditions are absent, indicate a tuberculous etiology. Normal values, however, do not exclude it. For the prognosis and the control of therapeutic measures it is unreliable. For the diagnosis and prognosis of tuberculosis in children the sedimentation rate is of no value.—*Über die praktische Verwertbarkeit der Senkungsgeschwindigkeit der roten Blutkörperchen für die Diagnose und Prognose der Tuberkulose im Kindesalter, C. Völckers, Beitr. z. Klin. d. Tuberk., 1924, lvii, 359.*—(*H. J. C.*)

Red-Cell Sedimentation Test.—In order to determine more exactly the sedimentation curve, it is studied at intervals of between 10 and 30 minutes in a Sahli hemoglobinometer tube and translated into a coördinate system. While the curve was straight in healthy individuals, in pathological cases there were characteristic deviations. Inactive cases of tuberculosis differentiate themselves from active cases by the absence of these deviations. The deviations are greatest the more widespread and progressive the existing lung process. The effect of therapeutic measures can be followed by utilizing this curve.—*Eine Methode zur genauen kurvenmässigen Darstellung der Blutkörperchensenkungsgeschwindigkeit, G. Peschel, Beitr. z. Klin. d. Tuberk., 1924, lviii, 195.*—(*H. J. C.*)

Red-Cell Sedimentation Test.—The sedimentation rate of red blood corpuscles is not an absolutely certain diagnostic method for activity of pulmonary tuberculosis although in some cases it may prove valuable.—*Über die Senkungsgeschwindigkeit der roten Blutkörperchen bei Lungentuberkulose, G. Schellenberg and H. Naucke, Beitr. z. Klin. d. Tuberk., 1923, lvii, 81.*—(*H. J. C.*)

Red-Cell Sedimentation Test.—The method of Westergren-Katz was used. The determination of a tuberculous process is possible only to a limited extent. To classify the individual cases into their Turban-Gerhardt stages the sedimentation reaction is valueless. The activity or inactivity of a case can be fairly definitely determined by means of the reaction. The main value of the reaction lies in the determination of the intensity of the process. The reaction furnishes a certain index for prognosis.—*Der Wert der Senkung der roten Blutkörperchen für die Diagnose und Prognose der Lungentuberkulose in graphischen Dartstellungen, O. Zöckler, Beitr. z. Klin. d. Tuberk., 1924, lvii, 293.*—(*H. J. C.*)

Red-Cell Sedimentation Test in Children.—After 1500 tests, by the method of Westergren, on 500 children, it is concluded that the sedimentation rate is not a specific reaction for tuberculosis, but is a valuable aid in differential diagnosis. It is also valuable in determining activity, which always goes hand in hand with a high sedimentation rate. From a prognostic standpoint the sedimentation rate is only of slight value, unless it shows persistently high or low values. It is also valuable in determining the benefit being derived from specific treatment.—*Die Senkungsgeschwindigkeit der Erythrocyten bei der Tuberkulose des Kindes, H. Rennebaum, Beitr. z. Klin. d. Tuberk., 1923, lvii, 263.*—(*H. J. C.*)

Tuberculosis of Ethmoid Cells.—The patient had a bilateral dacryocystitis complicated by nasal and conjunctival tuberculosis. Extirpation of the lachrymal sacs revealed extensive lesions of the lachrymal groove and of the anterior ethmoid cells. These lesions, as well as the conjunctival vegetations, were successfully treated by diathermo-coagulation. The tuberculous

nature of the lesions was proved by microscopic examination, guinea-pig inoculation, and the reaction of Besredka. Tuberculous ethmoiditis is rare.—*Tuberculose végétante de la conjonctive et des voies lacrymales d'origine sinuso-nasale. Traitement par la diathermo-coagulation, G. Worms and Blanchard, Meeting, Soc. d'Ophthalmologie de Paris, December 20, 1924, reported in Presse Méd., January 18, 1925, no. 5, 73.*—(*J. B. A.*)

Heliotherapy in Tuberculosis of Epiglottis.—The classical treatment of tuberculous infiltration of the epiglottis up to the present time has been puncture with the thermocautery. This transforms a closed into an open lesion. The inflammatory reaction which follows produces dysphagia, and the patient dies of inanition. Heliotherapy is recommended in this condition. The indications vary, depending on whether the epiglottis alone is involved, or whether it is complicated by involvement of the vocal cords. In the first instance heliotherapy is begun before applying the galvanocautery. In the second cauterization is contraindicated. The aggravation of the local and general condition by the cauterization shows that heliotherapy alone may be recommended before any other treatment in a tuberculous infiltration of the epiglottis.—*L'indication de l'héliothérapie dans l'infiltration tuberculeuse de l'epiglotte avant tout autre traitement, Kowler, Congrès Francais d'Oto-rhinolaryngologie, October, 1924, reported in Presse Méd., November 1, 1924, no. 88, 865.*—(*B. T. McM.*)

Interlobar Pleurisy and Pulmonary Tuberculosis.—The patient, a woman, had a right interlobar pleurisy with a ruptured abscess which healed, but was followed two months later by the development of a right apical tuberculosis and the appearance of tubercle bacilli in the sputum. The lung was collapsed by artificial pneumothorax, and a good clinical result was obtained, until a new interlobar pleurisy developed, this time on the left. Despite this, pneumothorax was continued, and the left pleurisy healed as the first one had.—*Pleurésie interlobaire suive de réveil d'une tuberculose pulmonaire du meme côte et de pleurésie interlobaire du côte opposé, E. Rist, meeting, Soc. Méd., des Hôp. de Paris, December 12, 1924, reported in Presse Méd., December 17, 1924, no. 101, 1009.*—(*J. B. A.*)

Gross Hilar Adenopathy in Adult Tuberculosis.—Recently the diagnosis of tracheobronchial adenopathy has been subjected to severe scrutiny and criticism, which includes also the radiographic findings under cover of which some of these diagnoses are made. There is a tendency to regard tracheobronchial tuberculous adenopathy as belonging exclusively to childhood, and some even question its existence in adults. The facts gathered during the war, however, especially among the black troops, indicate not only that it exists in adults, but may even attain considerable proportions. The notion of tuberculosis in relation to age must be modified as it is really a question of primary infection or reinfection, of virgin or allergic soil. Most childhood tuberculosis is a tuberculosis of first infection, and is accompanied by an exuberant lymphatic reaction. Most adult tuberculosis, being a tuberculosis of reinfection or reactivation, manifests itself in a different way. But if an adult who has previously escaped the many opportunities of infection is subjected to a sufficiently massive inoculation, he will react like the child. The group of cases of special interest, then, to phthisiologists is that of young adults with "gangliopulmonary tuberculosis." The subjects had passed their childhood in the country and developed their first tuberculosis symptoms soon after moving to the city. In all, the clinical and radiological signs were in perfect accord, leaving no doubt of the nature of the affection, or of the predominantly adenopathic character of the lesions. In two cases final proof was had at autopsy; in several the bacilli were found in the stools, and in one in the sputum. Attention is drawn, however, to a too widespread error in radiographic interpretation of denominating as "hilar adenopathy" all the more or less confluent, arborescent or nodular shadows which almost every one presents in the hilar region, and which may perfectly well be due to blood vessels or bronchi. Among the prominent symptoms presented in the cases studied were dry spasmodic cough, general fatigue, febrile exacerbations, loss of weight and strength, anemia, and amenorrhea. Expectoration is usually absent, and there is frequently no cough; hence the finding of bacilli in the stools is most valuable corroborative evidence, though scarcely necessary for the diagnosis. Among the chief physical signs noted were bronchial breathing over the hilum, transmitted outward feeble or muffled breathing, bronchial voice and whisper, paravertebral dulness, exaggerated fremitus, and, more rarely, dry crepitations. Radiographic examination shows distinct nodular densities or massive opacities in the hilar region, extending more or less into the lung field, frequently unilateral. In one case autopsied the lymphatic mass penetrated like a wedge into the lung, which was sown with disseminated miliary pneumonic foci. Six case

reports are included, with illustrative X-ray pictures.—*Les grosses adénopathies hilaires dans la tuberculose de l'adulte. La tuberculose gangliopulmonaire du "jeune adulte," E. Sergent, H. Durand and P. Cottenot, Rev. d. l. Tuberc., October, 1924, v, 593.—(A. P.)*

Ileocecal Tuberculosis.—Primary intestinal tuberculosis is rare. When it does occur, it is most common in young people, under 18, and is probably of bovine origin. In the adult it is usually secondary to tuberculosis of the lungs or bronchial lymph nodes. The hyperplastic form of intestinal tuberculosis is due to a relatively mild infection. It is usually seen in the cecum and sigmoid, with the appendix as the most likely seat of the original process. In such cases the mesentery is thickened, the appendix large, and both stand out prominently as a pinkish mass resembling a badly infected granulating finger. The involvement of the cecum varies with the duration of the infection. In some cases the ceco-appendix forms a tumor-like mass. Secondary infections of the bowel probably originate in the lower ileum, extending by way of lymphatic channels (and possibly by direct extension) to cecum, colon, duodenum, and even stomach. We have available symptoms and signs, the presence of tubercle bacilli in the stools, the X-ray, and the tuberculin test, for diagnosis. The finding of bacilli in the stools and the tuberculin test are of little practical value in the presence of pulmonary tuberculosis, and unfortunately 79 per cent of ileocecal tuberculosis is secondary to pulmonary or lymphatic disease. X-ray diagnosis also has its limitations. The so called "filling defects" are in most cases merely irregular fillings due the spasm associated with ulceration, and are not constant. Fluoroscopy is very useful in showing this, and palpation of the abdomen during fluoroscopy should be practised. In many cases the diagnosis rests largely on the symptoms, the chief of which are pain in the abdomen, usually centering around the umbilicus and extending to the left side, indigestion with gas, loss of appetite and weight, fever, constipation and fulness after eating, and lastly diarrhea. Diarrhea is generally a late rather than an early symptom, and does not occur until the colon is extensively involved, because when the colon is normal it holds the fluid contents until the water is absorbed, even though the small intestine empties rapidly into the cecum. Irregular peristalsis and colicky pains are much more significant, and a dull aching pain in the right side, at times colicky, is the most common symptom in ileocecal tuberculosis. There may also be observed in these patients a peculiar doughy feeling of the abdomen. When these cases can be diagnosed early they are entirely amenable to surgical therapy, and a careful ether anesthesia is not contraindicated by the presence of pulmonary tuberculosis. A wide resection of the diseased intestine is the operation of choice, together with the attached mesentery and lymph nodes, if these are involved, as is usual. Three cases are cited, in two of which the results were most satisfactory and in one, a girl of 11, truly remarkable. This last case began with the symptoms of an acute appendicitis, the true condition being discovered after laparotomy.—*Ileocecal Tuberculosis, J. M. Lynch, J. Am. M. Ass., January 3, 1925, lxxxiv, 24.—(A. P.)*

Intestinal Tuberculosis Complicating Pulmonary Tuberculosis.—This paper adds nothing new to the authors' articles on this subject already published in English. The numbers of cases examined has increased to 1614 without any marked difference in the incidence of this complication. Conviction becomes constantly stronger that the X-ray method of diagnosis, and treatment by heliotherapy and X-ray are great steps in advance.—*Étude sur la tuberculose intestinal chez les tuberculeux pulmonaires. Radiodiagnostic traitement, L. Brown and H. L. Sampson, Ann. de. Med., November, 1924, xvi, 381.—(W. B. S.)*

Atony of Stomach in Tuberculosis of Lung Hilum.—In a large number of cases in which organic lesion of the stomach was suspected on the basis of symptoms, roentgenological examination detected no abnormality except gastroptosis. This was often of marked degree. In 316 cases in the author's experience this was associated with an old tuberculosis in which the lung hilum had been involved. A constant finding was a very low position of the lower pole of the stomach and greater curvature, the stomach itself being wide and slack. A quite similar condition has been produced experimentally by Klee in decerebrated cats on interference with the vagus nerve. In these animals the muscular tone of the stomach is so reduced that little resistance is offered to incoming food, and the stomach promptly sags. In human beings with this type of stomach the collapsed walls of the upper third of the fasting stomach are opened by the test meal. The meal falls to the lower part of the stomach, converting the caudal region to a broad, roomy sack. The ascending portion is small and sharply contracted. Leb believes the association of the involvement of the lung hilum with the atonic condition of

the stomach is one of cause and effect. It has been shown that tuberculous lesions of the lung hilum and mediastinum may affect the nearby vagus nerve. The physiological effect of such injury would be depression of the motor function of the stomach, with preponderance of the sympathetic. The immediate effect would be followed by in-increasing dilatation and anatomic fixation in the new position.—*Eine durch Tuberkulose des Lungenstieles bedingte Form der Magenatonie, Leb, München. med. Wchnschr., October 31, 1924, lxxi, 1527.*—(*E. R. L.*)

Abdominal Tuberculosis and Intestinal Stasis.—Arbuthnut Lane stated that there was no tuberculosis without previous intestinal stasis. Taylor believes that any delay in emptying the bowel becomes a serious predisposing factor in abdominal tuberculosis and that the fault is primarily in the colon, where nature, attempting to prevent ptosis, develops certain bands, following which the bowel becomes kinked. He believes that toxemia results from absorption which has a "devitalizing" effect on the tissues. It is true that the symptoms usually complained of in abdominal tuberculosis are a too rapid emptying of the bowel, but doubtless if one could have X-rayed them before tuberculosis became apparent actual delay would have been shown. The cases discussed are those ordinarily known as tuberculous peritonitis of the adhesive type, with the mesenteric lymph nodes affected in some. Of 24 patients operated on, 7 showed such extensive adhesions that it was impossible to examine the relations of the different parts of the bowl, but when this was possible the greatest degree of obstruction was found at the points described by Lane, one under the pelvic colon, the other at the terminal ileum. The operation performed was a careful division of the bands, freeing the bowel, allowing the fixed loop to become straight, and accurately suturing the peritoneum over the raw surfaces; also removing the appendix, if fixed. The gastric symptoms have been seen to disappear entirely after division of the bands at the terminal ileum and pelvic colon. The older patients usually obtained the most relief.—*Abdominal Tuberculosis and Intestinal Stasis, J. Taylor, Med. J. & Rec., January 7, 1925, cxxi, 27.*—(*A. P.*)

Ultraviolet Light Therapy in Peritoneal and Lymphatic Tuberculosis.—This study is based on observations made on 10 cases of various forms of tuberculosis treated by the Alpine lamp. The literature on the subject is briefly reviewed. Full reports on the 10 cases are given. *Conclusions:* 1. The sole use of ultraviolet rays, as produced by the quartz-mercury-vapor arc lamp, has been of decided value in the treatment of peritoneal, lymphatic, and osseous tuberculosis. 2. Of the lymphatic forms of tuberculosis, the mesenteric is most rapidly improved, next the mediastinal, and last the peripheral. 3. Pulmonary tuberculosis of the miliary type remains wholly unifluenced by ultraviolet ray therapy, even though it is begun early in the course of the disease.—*Ultraviolet Ray Therapy in Peritoneal and Glandular Tuberculosis of Children, H. J. Gerstenberger and S. A. Wahl, J. Am. M. Ass., November 22, 1924, lxxxiii, 1631.*—(*B. T. McM.*)

Specific Bacteriotherapy of Surgical Tuberculosis.—In 1900 Vaudremer and Martin demonstrated the existence of a tuberculous poison different from tuberculin, able to kill guinea pigs by intrameningeal and intraperitoneal injection. This poison is obtained only from old cultures, or from younger cultures by washing in the Soxhlet apparatus with petroleum ether, which causes the bacilli to lose their acid-resistant character. Inoculation of 0.4 cc. of a weak emulsion of this bacillary extract under the arachnoid killed a guinea pig in less than twenty-four hours. Sublethal doses, on the other hand, increased their resistance to tuberculous meningitis or peritonitis. General vaccination could not, however, be employed because of reactions and hypersensitiveness, which were thought to be due to some contained tuberculin. It was attempted to remove this substance by prolonged maceration of the bacilli at 38°C. Animals treated with extract from these macerated bacilli after infection invariably long outlived the controls. *Technique:* The bacilli used were a mixture of human and bovine cultivated on glycerine-bouillon. When the culture was a month old the growth was removed and macerated in the filtered culture medium of *Aspergillus fumigatus* (for the purpose of utilizing the proteolytic and lipolytic ferments produced by this mold). After a month at 38°C. the bacilli were decanted, ground in a sterile mortar, taken up in distilled water, placed in ampules, and heated five minutes at 100°C. The emulsion prepared was very faintly opalescent. Doses of 1 to 1.5 cc. were used subcutaneously in patients with surgical tuberculosis, especially with cold abscess and sinus formation. Cultures from these on potato bouillon, to which 2 per cent gelatin has been added, show varied bacillary forms, especially granular non-acid-fast forms which take the Gram stain. These granular forms, killed at 36°C., may be used

to prepare an autogenous vaccine. Observations made on some 15 treated cases are cited, covering articular, bony and tendinous tuberculosis, also epididymitis, adenitis and serous membrane tuberculosis. Most of them had cold abscesses and fistulae and many had a complicating pulmonary tuberculosis. *Conclusions:* It is possible to check the evolution of surgical tuberculosis by subcutaneous injection of bacilli almost deprived of acid-resistance, deprived of tuberculin, and killed by heating. Serological investigations are being carried out to supplement the clinical observations which seem to show almost uniformly favorable results.—*Essais bactériothérapiques dans les tuberculose chirurgicales, A. Vaudremer, Presse Méd., October 8, 1924, no. 81, 801.—(A. P.)*

Bone and Joint Tuberculosis.—By employing such methods of study as (1) injection of blood vessels with a metallic substance casting a shadow with the X-ray and followed by roentgenograms, (2) injection of blood vessels followed by clearing of the bone by the Sphalteholz method and (3) making of reconstruction models from serial sections, a good idea of the anatomy and the blood supply of bone and joint has been reached. The work gives a good idea of the pathology and pathogenesis of skeletal tuberculosis, especially as it is concerned with the spine, hip, knee, shoulder and costal cartilages. These anatomical studies were done on material from the newborn infants and young individuals. In the spine the intervertebral disc is without blood vessels; the epiphysis has blood vessels that extend from the main vessels of the vertebral body but no independent vessels; the vertebral body is supplied chiefly by independent vessels which enter it from beneath the anterior longitudinal ligament. There is thus a parallelism between the incidence of tuberculosis in the various portions of the spine and the presence and number of blood vessels. The relationship between tuberculosis of the shoulder and the arrangement of the blood vessels is likewise evident from anatomic study. Many fine "end" vessels are distributed to the *sulcus bicipitis humeri*, the site in which the primary focus of tubercle of the humerus is usually seen. Tuberculosis of the knee manifests itself first, in the epiphyses of the femur in 59 per cent, in the epiphyses of the tibia in 34 per cent, and in the patella in 7 per cent, but the anatomical study in this connection concerned itself with only the blood supply of the lower end of the femur. Tuberculosis of the end of the bone is most commonly found in the lateral epicondyle, next in the medial epicondyle and least frequently in the intercondyloid notch. These structures possess a richness of vessels just in accordance with the frequency of disease: the largest number of vessels in the lateral epicondyle and fewest in the notch. Seventy-nine per cent of all inflammatory conditions of the hip are tuberculous. Tuberculosis is generally osseous in children and synovial in adults, and in children the epiphyseal vessels are end vessels while in adults the vessels anastomose abundantly. The same relation between abundance of vessels and loci for tuberculosis exists in the hip and, to some extent, in the costal cartilages as in other joints and bones. From these experimental data it seems fair to conclude that bone and joint tuberculosis is usually embolic in origin. Trauma and strain (seen especially in the case of the spine, hip and knee which carry the weight of the body) are not to be ignored as potent factors that contribute to the etiology of bone tuberculosis.—*A Contribution to the Knowledge of Pathogenesis of Skeletal Tuberculosis, A. Kolodny, J. Bone & Joint Surg., January, 1925, vii (old series xxiii), 53.—(H. S. W.)*

Pott's Disease with Mediastinal Abscess and Spastic Paresis.—The patient, a man of 63, was referred on account of intercostal pains and spasmodic cough. The onset of symptoms was in July, 1923, with right-sided thoracic pain, quite severe and radiating anteriorly. In September similar pains appeared on the left side. In December, 1923, the patient experienced a sense of thoracic constriction, especially on the right. In January, 1924, there appeared a dry cough, which assumed a spasmodic character and became very persistent. The patient also complained of a slight interscapular pain, and, for several days prior to being seen at the clinic, of slight paresis of the lower limbs, especially the left, with dysuria and constipation. Examination of the thorax was practically negative. Examination of the nervous system showed a spastic paresis of the lower extremities with exaggerated reflexes, ankle clonus and Babinski's sign. There was also a hypoesthesia of the lower extremities and trunk. These findings suggested medullary compression. Examination of the vertebral column showed slight dorsal kyphosis. Vigorous lateral movement of the spinal column provoked slight pain at the level of the fifth thoracic spine, which was also sensitive to deep and prolonged pressure in vertebral decubitus. Radioscopic and radiographic examination showed on the right an opaque massive shadow lateral to the superior venous trunks, extending from the upper border of the clavicle to the right

auricle, merging with the vertebral shadow mesially and encroaching on the pulmonary field laterally. Such a mediastinal lesion suffices to explain the spasmodic cough by vagus irritation. A left posterior oblique picture showed clearly an angulation of the vertebral column between the fifth and sixth thoracic vertebrae, and a semi-opaque mass occupying the intercardiovertebral space, extending anteriorly to the heart and posteriorly to the scapular shadow. A picture centered on the vertebral column posteriorly showed a cupping between the fifth and sixth thoracic vertebrae, with almost complete disappearance of the intervertebral disk, together with bony bulging. The angular curvature, the cupping, and disappearance of the disk are the signature of Pott's disease, and the mediastinal shadow represents an abscess. Senile vertebral tuberculosis is usually characterized by the absence of gibbus, the slight pain on pressure, the tendency to extension toward the surface, and termination by miliary tuberculosis. The nervous symptoms may be the first to reveal the presence of the bony lesion. Mediastinal abscess is not an especially rare complication, and may burst into a bronchus. The radiographic shadows are connected to the vertebral column in the form of a spindle or funnel. Some years ago it was thought that vertebral tuberculosis produced always bony rarefaction, in contradistinction to syphilis, but recent observations have disproved this. Neoformations have been recorded more often in the old than in the young.—*Mal de Pott du vieillard à symptomatologie médiastinale: parésie spasmodique, spondylose vertébrale associée, H. Roger and Huguet, Progrès Méd., August 23, 1924, no. 34, 511.*—(*A. P.*)

X-Ray Treatment of Bone and Joint Tuberculosis.—The results of roentgen treatment for the years 1911 to 1920 at the Kiel Surgical Clinic are reviewed. The report covers 362 of a total of 669 cases which were treated for a sufficiently long time (at least 2 years). As a whole the results with cases having fistulas were not much worse than for other forms. The evaluation of the roentgen action is naturally difficult, since all the other conservative methods were also used. The general impression is, however, favorable to the roentgen treatment. Small doses should be the rule. The danger of epiphyseal harm is slight with careful dosage. The drawbacks to the treatment are the time required, and the danger of delayed wound-healing should an operation be required in the rayed area.—*Über die Erfolge der Röntgenbehandlung der Knochen und Gelenktuberkulose, O. H. Petersen and Johanna Hellmann, Deutsche Ztschr. f. Chir., 1924, clxxxv, 230.*—(*H.J.C.*)

Treatment of Lupus with Copper.—*Kupferdermasan* has a number of advantages in the treatment of lupus. It has a selective affinity for lupus tissue, is easily applied, causes little pain, furnishes a substitute for light treatment, and is a valuable prophylactic against the spread of the infection when it is applied in the zone around the area of lupus.—*Beitrag zur Lupus-behandlung mit Kupferdermasan, G. Bettin, München. med. Wchnschr., September 5, 1924, lxxi, 1242.*—(*E. R. L.*)

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